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## GUIDE

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Deaths from Sickle Cell Disease in Intensive Care Units
Can we do better?

Lamk Al-Lamki

In this issue of the journal, Dr. Qutaiba Tawfic and his colleagues report their experience with sickle cell disease patients (SCD) who were admitted to the Intensive Care Unit (ICU) at Sultan Qaboos University Hospital, Oman, with various complications of sickle cell disease. They studied 49 patients who were admitted 56 times in the ICU between the years 2005 and 2009.1 This is an important study which has several points worthy of reflection. There is very little literature specifically discussing the subject of SCD patients who are admitted to an ICU for any SCD related complication. The literature typically deals with specific complications of SCD, like the acute chest syndrome (ACS), vaso-occlusive disorder and stroke in these patients, as well as their precipitating factors and their management.2–5

The mortality among Tawfic et al.’s, patients admitted to the ICU was 16%. They pointed out that this figure was lower than the general mortality rate of 21.1% in that ICU.1 However, this is not much of a consolation, and it is far from being a reason to rejoice. A typical patient admitted to an adult ICU, for problems other than SCD, is generally older than the patients who were the subject of this study. Patients in this study had a median age of only 27 years and the oldest patient was 52 years old. Therefore, the mortality of these patients cannot be compared to the mortality of the general adult ICU patients. The 16% mortality rate is indeed alarming for such a young population and should not be readily accepted. It should be a wake-up call as here we are dealing with a hereditary blood disorder, a killer disease of young adults. The situation is probably much worse than that if we include the number of children dying from complications of SCD in paediatric ICUs across this country, and in the general medical and paediatric wards. Child statistics were not included in this study, which only investigated adults SCD sufferers admitted to the ICU. The number of children who die in Oman from SCD is not clear and needs further studies. How many other children and adults die from SCD in their homes in Oman? We truly need to exert a more concerted effort to find out the basic facts about this disease in Oman. Medical researchers need to stop and ponder about the impact of this devastating disease on our society. This needs the full attention of the government in general, the health services in particular and more expectations from patients and non-governmental organisations (NGOs). We need answers!

Unfortunately, in the Western world, SCD is relatively rare and, hence, there is limited interest in research into this disorder. As a result of the low incidence, it has neither drawn the attention of researchers nor stimulated pharmaceutical companies to fund SCD research. There were
a number of clinical research studies on SCD published from the United States in the 1990s, many of them in reputable journals like New England Journal of Medicine, and other Western journals, but there were very few basic research studies into this disease. This was followed by a relative lull in the 2000s, when there was even less research published on the subject. Interest had probably waned for above-mentioned reasons. Earlier clinical research on SCD was into the major complications such as ACS, vaso-occlusive disorder, fat embolism, etc. and how to manage them. Unfortunately, these studies, though worthwhile, contributed little to the basic understanding that is needed to reduce SCD mortality in countries such as Oman where it is prevalent. Thus, Oman and the other Arab countries need to be more proactive and themselves undertake research into inherited blood disorders such as SCD. This would ultimately reduce not only mortality and morbidity, but also lessen the social and cultural impact of these diseases. For example, relationships can be disrupted and marriage plans destroyed because of the fear that a potential partner has the sickle cell trait or disease.

Tawfic et al. have shown that ACS is the most common cause of death in their group of patients. This is not an altogether new finding, but nonetheless interesting. It is well known that ACS is the second commonest cause of SCD admissions after painful crisis, and it is the prime cause of death killing around 30% of SCD patients. Even though ACS was described approximately 20 years ago, and repeatedly studied by others, we have not advanced much in either managing this condition, preventing it or dramatically reduce its effect, at least not in Arab countries. An aetiological contributing factor to ACS is fat embolism, yet little research is gone into preventing or combating that condition, although there is some evidence that hydroxyurea can reduce the recurrence of ACS, and reduce its severity.

Other patients die of acute stroke, commonly a result of vaso-occlusive disease. Again, we physicians as the health guardians of our communities have failed our societies by allowing ourselves to remain in the dark with respect to the disorders that lead to fat embolism, vaso-occlusive disorders, acute stroke and ACS, or other complications of SCD. We have achieved some progress in infection control, which is another major contributing factor to the mortality of SCD, and we do use the current preventative treatment with hydroxyurea. All these complications were present in the patients studied by Tawfic et al.

In the USA, the prevalence of heterozygous carriers of the sickle cell trait is 8% among the African Americans. This has lead Bruce Mitchell to summarise the frustration on the current lack of relevant SCD research in USA very concisely: “That is where we are: inconclusive data have been accepted; inconsistent messages about screening, prevention and precaution have been relayed; and research into sickle cell trait-associated sudden death has not advanced. For many physicians, the story stops there.” Typically, patients with sickle cell trait have about 40% of their haemoglobin as haemoglobin-S, but they do not have anaemia and so are able to live a normal life. Unfortunately, that is not always the case in Africa where life expectancy of the 6 million people with sickle cell anaemia is only half the normal life expectancy. The World Health Organization (WHO) has declared SCD a public health priority. “The WHO estimates that 70% of sickle cell anaemia deaths in Africa are preventable with simple, cost-effective interventions, such as early identification of sickle cell anaemia patients by new born screening and subsequent provision of comprehensive care such as giving regular prophylaxis such as penicillin V and vaccinations. Implementation of comprehensive care for SCD patients could lead to improved survival through these targeted interventions.” If 70% of SCD deaths are preventable in Africa with simple interventions, then we should be able to achieve a higher percentage in Oman with all the resources and potential that we have in Oman. If the WHO has declared sickle cell disease a public health priority in Africa, then why is it not one here in Oman? Certainly, we need to pause and ponder—what do we need to do in Oman for this public health priority and to reduce the mortality?

To start with we need early detection of the trait and of the symptoms of the disease. In Africa, haemoglobin-S trait is protective against malaria, morbidity and mortality, and hence, to some extent, it may protect some people from that disease. Although it may be that the sickle cell gene has come to Oman for the same reason, this country no longer has a major problem with malaria and therefore we can afford to rid of SCD. The prevalence of SCD in...
Oman is generally accepted as 6%.11,12 The incidence of the sickle cell disease itself has been reported at both 0.2%.12 Clearly, we need much more research to obtain more accurate statistics on both, the trait and the disease. Recent prospective data from our university hospital and Sohar hospital by AlKindi et al. indicates the incidence of SCD is about 0.3%.13

The Oman Hereditary Blood Disorder Association was established with the aim of improving services provided to patients with haemoglobin disorders in Oman, including on psychological and social levels.15 They raise awareness about hereditary blood disorders, including SCD, and their effects on the community. This Association involves both health professionals and patients and, while they are doing a commendable job, they need to be more active in lobbying for legislation on widespread testing and screening for hereditary blood disorders, and in calling for more research. The Research Council (TRC) of Oman is currently supporting one on-going research project on SCD. However, as we have seen, with a mortality rate of over 16% from SCD in one Omani ICU, we need much more basic research on the aetiology and management and, specifically, prevention of all the complications. The Association needs to work in concert with the Research Council and the Ministry of Health to reduce this mortality.

Western countries such as USA and UK have managed to lower their overall mortality from SCD (not only in the ICU) from 3% to 0.13 per 100 person years of observation.9 Surely, we need to do even better because of the impact this condition has on our society. Our doctors have the know-how but we need more support from the NGOs, the public and the Ministry of Health. Oman is spending one of the lowest percentages of gross domestic product (GDP) on health care, compared to most of the world—only just over 2% of GDP, compared to 6–12% in other countries and 17.4% in the USA.14,15 Oman needs to invest more money to support and improve our health system and reduce mortality from SCD and other hereditary blood disorders. Our health care investment levels should not remain at about the lowest in the Gulf region, and much lower than most other countries.

So what is the effect of this low health care expenditure on SCD? To start with, if we had more ICU beds, then we might be able to admit patients earlier and therefore, reduce mortality. As indicated above, because there is very little in the world literature on ICU patients with SCD, we have no statistics to compare with our figure of 16% mortality, but general medical logic tells us that we should be able to lower this rate by earlier intervention and better preventative measures. Not only should doctors and the ministry be more vigilant, but also, the patients need to be better educated about the disease, e.g. by presenting themselves early to the doctor, as soon as they have symptoms that may suggest ACS, such as fever, shortness of breath or cough.

The paper published in the New England Journal of Medicine in 1994 studied 538 patients with SCD and ACS.9 Their mortality was lower with only 18 out of their 538 patients dying from ACS (3.3%). Certainly, this would indicate that mortality from ACS can be reduced with adequate and early medical intervention which implies greater expenditure and investment in our health services.

In 1999, the National Institutes of Health in the USA published suggestions for preventing morbidity and mortality from SCD, from which we could learn several lessons and develop more research.16 Likewise, the Harvard study17 and the Sultan Qaboos University studies18,19 also offer some ideas which, hopefully, could stimulate the Oman Hereditary Blood Disorder Association and The Research Council to get together and do some similar research on SCD. Overall, we need much more research on this genetic disorder, like many other genetic disorders in Oman and in the Arab world.20 We have to shoulder this responsibility ourselves as we cannot wait for, or rely on, pharmaceutical companies or Western countries to do this research for us. Yes, we can, and we must do better in Oman.

References


Over the past decade substantial advances have been made in understanding the biological and molecular mechanisms of chronic lymphocytic leukaemia (CLL). The evaluation of new chemotherapeutic combinations has led to an increase in the rate of complete remission in patients with CLL. In addition, the use of monoclonal antibodies such as rituximab and alemtuzumab has added substantial benefit when combined with chemotherapy.1,2 However, the ability to eradicate disease at a molecular level, and improve clinically relevant patient outcome measures, continue to pose difficult challenges. Regardless of the stage of the disease, most patients will relapse after initial treatment and become refractory to salvage chemotherapy with median overall survival ranging from 10 to 19 months.3,4 Thus, the need to develop alternative therapies to kill leukaemic cells, or to fight relapse, remains a hot topic under intense investigation. Targeting cell-surface molecules present on leukaemic B-cells with T-cells transfected with chimeric antigen receptors (CAR) may be an attractive immunotherapeutic strategy to reduce the leukaemic cell burden.

CAR can be engineered by combining an antigen-specific monoclonal antibody using its variable chain fragments with a T-cell activating signalling receptor in a single fusion protein.5 Once this modified protein is expressed on the surface of a T-cell, and binds to its specific antigen, an activation signal is transmitted into the T-cell. This latter will trigger its effector functions to lyse the target cell. Typically, T-cells expressing CAR react like conventional T-cells, but attach to the target antigen by the variable chain fragments of the monoclonal antibody, and so are named T-bodies.

Since its first description, CAR design has evolved over the years with the goal of enhancing T-cell signalling functions [Figure 1]. The first generation of CAR consisted of heavy and light chain immunoglobulin variable regions fused in a single chain and coupled to signalling modules, which are normally present in the T-cell receptor complex such as the CD3zeta-chain.6 This first generation of CAR effectively redirected T-cell cytotoxicity, but failed to enable T-cell proliferation and survival upon repeated antigen exposure, and anti-tumour responses were limited.7 The second generation of CAR incorporated another signalling receptor from co-stimulatory molecules such as CD28, CD134 or CD137 to reduce activation-induced cell death and improve T-cell survival. The third generation of CAR incorporated two co-stimulatory molecules: CD28, CD134 or CD137 in a sequence fused to CD3-zeta chain and were designed to further enhance killing functions, proliferation capacities and production of survival cytokines such as interleukin-2.7,8 Compared to classical T-cell-based immunotherapies, T-cells expressing-CAR present several attractive advantages including obviating the need for recognising peptide presentation by major histocompatibility complex, the ability to target a range of tumour surface antigens, and relatively

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A New Cellular Weapon to Kill Leukaemic B-Cells

rapid generation within one to four weeks.\textsuperscript{5,7,8} Although the clinical value of genetically engineered T-cells is still to be validated, recent data from two studies reported that CAR targeting CD19 (CART19) was able to kill leukaemic B-cells expressing this surface antigen and that tumour control was sustained for 10 months following this therapy.\textsuperscript{9,10} The CART19 was designed to express a single chain variable fragment derived from an anti-CD19 specific antibody along with a CD137 signalling domain and the CD3\textsuperscript{zeta}-chain. T-cells expressing CART19 were generated by transfecting autologous T-cells from each CLL patient with a lentiviral vector, which express the CART19 construct. Prior to receiving a low dose of CART19, patients received lymphodepleting chemotherapy with pentostatin and cyclophosphamide and, 4 days later, \(1.42 \times 10^7\) of engineered CART19 cells were administrated without additional cytokines or monoclonal antibodies. Two to three weeks after CART19 immunotherapy, patients developed a tumour lysis syndrome, which correlated positively with an increase in the number of circulating T-cells expressing CART19. Three to four days later the tumour lysis syndrome subsided without evidence of disease on physical examination. There was no palpable adenopathy and no evidence of CLL in the bone marrow. In addition, computed tomography (CT) scans showed a resolution of adenopathies. Six to 10 months following CART19 infusion, two of three subjects showed a complete remission with no residual CLL found by means of physical examination, CT scans, flow-cytometry and cytogenetic analyses. Normal B cells however continued to be lacking. Of note, each infused CART19 cell eradicated on average about 1,000 malignant cells. T-cell expressing CART19 underwent robust expansion, persisted at high levels in both circulating blood and bone marrow for at least 6 months and, most importantly, a proportion of these T-cells expressed memory markers and retained anti-CD19 effector functions. As expected the most frequent side effects, in addition to the tumour lysis syndrome, were B-cell lymphopenia and hypogammaglobulinaemia but these undesirable conditions should be manageable in CLL patients.

Overall, these small pilot, prospective, single-centre studies yielded very encouraging results as two of the three patients enrolled in the clinical trial had p53 gene deletion, which predicts poor survival, non-response to therapy and rapid progression. It also provides a proof of principle that CAR represents a promising approach to treat CLL patients and possibly other B-cell malignancies.\textsuperscript{11,12} Indeed, this therapy resulted in partial remission

\begin{figure}
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\caption{Simplified representation of chimeric antigen receptors (CAR) design. Generally, T-cells expressing-CAR consist of a single chain variable fragments (scFv) from a monoclonal antibody, a transmembrane region (TM) and signaling receptors such as CD3\textsuperscript{zeta}-chain domain (first generation), two signaling domains (second generation) or three signaling domains (third generation).}
\end{figure}
in a patient with follicular lymphoma for up to 32 weeks. In a more recent study, three patients with bulky CLL and one patient with B-cell acute lymphoblastic exhibited a response to CART19 containing CD28 as a co-stimulatory molecule.

Accordingly, CART19 is generating substantial enthusiasm and its clinical value will probably be evaluated in large clinical trials. However, one potential concern is that co-stimulatory signals may lead to uncontrolled CAR T-cell proliferation thereby increasing the long term risk of toxicity by depleting non-tumour cells, which are important for homeostatic functions. It remains to be seen whether the long term side effects of CART19 will be acceptable or not. Another major safety issue is the theoretical risk of inducing oncogenic mutations after DNA integration of the vector. Previous reports have shown the occurrence of T-cell acute lymphoblastic leukaemia in four children treated with gene-transfer stem cells to correct their X-linked severe combined immunodeficiency. However, in contrast to haematopoietic stem cells, retroviral vector integration to mature T-cells has been found to be a safe strategy as demonstrated by long-term engraftment of donor lymphocytes genetically engineered with the suicide gene thymidine kinase of herpes simplex virus after allogeneic stem cell transplantation.

Treatment with CART19 is an innovative immunotherapeutic approach to target leukaemic B-cells in patients with advanced chemotherapy-resistant CLL.

Certainly, this approach is still in its infancy for clinical use, but it constitutes a new weapon against B-cell neoplasms and potentially a model to further improve the curative potential of cellular therapies in patients for whom conventional therapies have failed.

References


Vitamin D Deficiency
This clandestine endemic disease is veiled no more

Moeness Moustafa Alshishtawy

Extracted Text:

vitamin D is not really a vitamin. 1 Vitamin D (which includes both D 2 and D 3 ) behaves like a hormone and carries out essential biological functions through endocrine, paracrine, and intracrine mechanisms. 2 Vitamin D 3 (ergocalciferol) is a synthetic product produced by irradiation of plant sterols, while vitamin D 2 (cholecalciferol) is a prohormone made in the skin in response to the action of ultraviolet (UV) B irradiation on a cholesterol precursor, 7-dehydrocholesterol. 3,4 When the skin absorbs UVB radiation, the precursor is converted to previtamin D 3 , which undergoes a thermally induced transformation to vitamin D 3 [Figure 1]. 3

A small part of vitamin D 3 comes from dietary intake, especially fatty fish (e.g. herring, mackerel, sardines, tuna, salmon), eggs, and fortified foods. 4,5 Thus, the major source of vitamin D is sunlight exposure. However, variables such as time of day, season, latitude, clothing, skin pigmentation, and age affect the amount of vitamin D converted in the skin. 6

ACCEPTED 12 th Feb

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Vitamin D, whether absorbed through the skin or consumed, is metabolised in the liver by 25-hydroxylase to 25-hydroxyvitamin D (25(OH)D), a prehormone form. In its endocrine action, 25(OH)D is converted by hydroxylation in the kidney to 1,25-dihydroxyvitamin D (1,25(OH)₂D), which circulates in the blood as a hormone to regulate mineral and skeletal homeostasis (Figure 1). In addition to the kidney’s endocrine production of circulating 1,25(OH)₂D, vitamin D
Vitamin D Deficiency
This clandestine endemic disease is veiled no more

In this system, 25(OH)D is converted to 1,25(OH)2D intracellularly by 25(OH)D 1-a-hydroxylases in a variety of end-organ tissues such as the prostate gland, breasts, colon, lungs, and keratinocytes [Figure 1].6 The conversion of 25(OH)D to 1,25(OH)2D in these tissues appears not to be controlled by calcium, but rather to be directly linked to the substrate availability of 25(OH)D. That is a complex endocrine reaction which begins in the largest organ of the body, the skin.7

In contrast to 1,25(OH)2D, which has a short half-life of ~4–15 hours, the serum concentration of 25(OH)D has a fairly long circulating half-life of ~15 days,6 and is considered the best indicator of vitamin D status that can be measured.8 Serum 25(OH)D reflects vitamin D produced cutaneously and also that obtained from food and supplements.7–9

Vitamin D Status around the World

Vitamin D status has been studied on all continents and in most countries throughout the world. In total, approximately 5,060 epidemiological studies have been done according to a PubMed search conducted in February 2012. These studies revealed that vitamin D deficiency was prevalent across all age-groups, geographic regions, and seasons.10–12

Despite ample sunshine, vitamin D deficiency is very common in the Middle East (15°–36°N) and African (35°S–37°N) countries.13,14 The first study to reveal low vitamin D concentrations in people of the Middle East region was conducted by Woodhouse and Norton in 1982 among ethnic Saudi Arabians.15 Their results were confirmed in 1983, when Sedrani et al. recorded a mean 25(OH)D concentration ranging between 10–30 nmol/L (2.496 nmol/L being equivalent to 1 ng/ml) among Saudi university students and the elderly.16,17 A more recent study that was conducted in the Eastern Province of Saudi Arabia revealed vitamin D deficiency (25(OH)D of ≤50 nmol/L) among 28–37% of 200 randomly selected healthy men.18 Another study, also conducted in the eastern regions of Saudi Arabia, showed low serum 25(OH)D concentrations among both males and females (25.25 nmol/L and 24.75 nmol/L, respectively) despite the fact that >65% of participants had adequate exposure to sunlight and >90% reported an adequate intake of dairy products.19

In Oman, according to the 2004 Ministry of Health survey, out of 298 non-pregnant women of child bearing age, 21.4% were found to be vitamin D deficient (<27.0 nmol/L).20 Almost half of the women included in the survey (47%) had serum 25(OH)D concentrations below 37.5 nmol/L, while only 10% of them had concentrations above 75 nmol/L.21 A more recent study tested serum 25(OH)D concentrations in 41 apparently healthy Omani women of childbearing age. The study indicated that all women had serum 25(OH)D concentrations of <50 nmol/L.22 Another study examined serum 25(OH)D concentrations in 103 healthy Omani pregnant women on their first antenatal visit to the hospital. The study revealed that 33% of cases had ‘at risk’ concentrations (25(OH)D <25 nmol/L), and that 65% had serum concentrations of 25(OH)D between 25 and 50 nmol/L, and not one case was found in the optimal range (25(OH)D >75 nmol/L).23

Similarly, vitamin D deficiency was found to be highly prevalent in the United Arab Emirates (UAE). Studying the efficacy of daily and monthly supplementation with vitamin D2 in lactating and nulliparous Emirati women, the results revealed that most women had vitamin D deficiency (25(OH)D ≤ 50 nmol/L at study entry).24 Also, Dawodu et al. investigated the effect of sun exposure at recommended levels on the vitamin D status of eight healthy Arab women of child-bearing age working in the Al Ain district of the UAE. Serum 25-hydroxyvitamin D concentrations were measured pre- and post-intervention. Although vitamin D concentrations remained suboptimal, median serum 25(OH)D concentrations were significantly higher post-intervention (23.0 nmol/L) than pre-intervention (17.6 nmol/L).25

A very recent study done by Anouti et al. in 2011 investigated a random sample of 208 young Emirati university students in Abu Dhabi, 138 females and 70 males. The mean serum 25(OH)D concentration for female students tested in April was 31.3 ± 12.3 nmol/L, while in October, it was 20.9 ± 14.9 nmol/L.26 This difference was statistically significant, suggesting that seasonal variation plays an important role in vitamin D status. Female students scored significantly higher than males on the sun avoidance inventory (SAI), indicating that females tend to avoid sun exposure to a greater extent than...
males, a possible explanation of the lower vitamin D status.26

In Qatar, the mean overall vitamin D concentration among health care professionals working at Hamad Medical Corporation in Doha, was found to be 29.3 nmol/L. Vitamin D concentration was lower in females (25.8 nmol/L) than in males (34.3 nmol/L). A total of 97% of all participants had a mean concentration <75 nmol/L, while 87% had a mean concentration of <50 nmol/L.27 In another study, vitamin D deficiency was prevalent (68.8%) among young Qatari children below 16 years of age, mostly in the age group 11–16 years (61.6%). Girls were affected more than boys (51.4% versus 48.6%).28

Even in north African countries there is a high prevalence of low vitamin D status: 25(OH)D is in the rachitic range. Veiled women, or women wearing purdahs (cloth that covers the whole of the body), have a lower vitamin D status than their peers within the same country.29 Studies in Turkey and Jordan showed also a strong relationship with clothing.30,31 Serum 25(OH)D levels were highest in women who wore Western clothing, decreasing in traditional women wearing a hijab (veil that covers the whole head except the face), and the lowest levels were measured in completely veiled women who wore a niqab (additional veil covering the whole face, or all of it except the eyes). Men in these countries have higher concentrations than women. In Iran, a population study that included 1,210 men and women between 20 and 69 years old, showed that the mean serum 25(OH)D was 20.6 nmol/L.32 In India, among 20 pregnant women in delivery at Sant Parmanand Hospital in Delhi, more than 75% were deficient in 25(OH)D (<50 nmol/L).33

Serum 25(OH)D concentrations are not only suboptimal in eastern or southern countries or specific risk groups, but also in adults in many Western countries.4 For instance, in the Netherlands, a study that assessed the prevalence of vitamin D deficiency in 358 pregnant women of several ethnic backgrounds living in The Hague, recorded that mean serum 25(OH)D concentrations in Turkish women were 15.2 ± 12.1 nmol/L; in Moroccan women 20.1 ± 13.5 nmol/L, and in other non-Western women 26.3 ± 25.9 nmol/L. These concentrations were significantly (P ≤0.001) lower than those in the Western women living in that country (52.7 ± 21.6 nmol/L).34 In the UK and elsewhere, vitamin D deficiency was found to be common among pregnant women.35

Most clinicians believe that vitamin D deficiency has been essentially eliminated in the USA, but recent data indicate that the diagnosis exists in epidemic proportions.36 Data from the National Health and Nutrition Examination Survey (NHANES) showed that the number of persons with 25(OH)D concentrations below 75 nmol/L nearly doubled between the 1994 and 2004 surveys, each of which extended for several years each.37 Data from the NHANES III 2004 survey showed that 65–75% of the population had 25(OH)D concentrations of <50 nmol/L.12 Less than 3% of African-American mothers were vitamin D sufficient, and the mean cord blood concentrations of 25(OH)D in their infants was very low (25 ± 15 nmol/L).37,38 More recent research from the USA also studied vitamin D concentrations in different ethnic groups, and included 154 African-American, 194 Hispanic, and 146 Caucasian women at <14 weeks of gestation. In logistic regression models, race was the most important risk factor for vitamin D deficiency or insufficiency. African-American women and Hispanic women were more likely to have vitamin D insufficiency and deficiency than Caucasian women.39 Also, Bodnar et al. conducted a study to assess, by race and season, the vitamin D status of pregnant women and their neonates residing in Pittsburgh. The serum 25(OH)D of 200 white and 200 black pregnant women was measured throughout gestation (4–21 weeks), previous to delivery, and in the cord blood of their neonates. The results suggested that black and white pregnant women and their neonates residing in the northern USA were at high risk of vitamin D insufficiency.40

Thus, it seems that the world is facing today what is, in fact, a new endemic disease that was, until recently, totally veiled. The actual percentage of vitamin-D-deficient people seems to be far greater than reported, so identifying the reasons for the dramatic increase in vitamin D insufficiency is not an easy task.

**Vitamin D Deficiency - Causes and Questions**

Declines in 25(OH)D concentrations are usually the result of dietary inadequacy, impaired absorption and use, increased requirements, or increased
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The upward trend in body mass index is also accused of causing vitamin D deficiency, and obesity is now added as a major contributory factor to the increasing prevalence of vitamin D insufficiency. Genetic predisposition may also have an effect on vitamin D blood concentrations and it has to be accounted for in the design of preventive measures against vitamin D deficiency.

A recent work by Grant aimed to estimate the reduction in mortality rates for six geopolitical regions of the world. It was based on an interpretation of the journal literature relating to the effects of solar UVB and vitamin D in reducing the risk of vitamin D-sensitive diseases. Six major diseases that account for more than half of global mortality rates (i.e. cardiovascular disease (CVD), cancer, respiratory infections, respiratory diseases, tuberculosis and diabetes mellitus) were studied in addition to vitamin D-sensitive diseases and conditions that account for 2–3% of global mortality rates such as Alzheimer’s disease, falls, meningitis, Parkinson’s disease, maternal sepsis, maternal hypertension (pre-eclampsia) and multiple sclerosis. The study showed that increasing serum 25(OH)D concentrations from 54 to 110 nmol/L would reduce the vitamin D-sensitive disease mortality rates by an estimated 20%. The reduction in all-cause mortality rates ranged from 7.6% for African females to 17.3% for European females. Reductions for males were on average 0.6% lower than for females. The estimated increase in life expectancy was 2 years for all six regions.

Why should we be concerned about Vitamin D Deficiency during Pregnancy?

Generally, there are many important health benefits from vitamin D for both mother and fetus. However, new clinical research results over the past decade indicate that appropriate intakes of vitamin D may provide greater health benefits than previously thought, benefits that include not only improved bone health, but other effects as well. Recent data suggest that 1,25(OH)2D aids implantation and maintains normal pregnancy. It also supports fetal growth through delivery of calcium, controls secretion of multiple placental hormones, and limits

Why is Vitamin D so Important?

Vitamin D is much more than a nutrient needed for bone health; it is an essential hormone required for the regulation of a large number of physiological functions. Its receptors were found to be present in nearly every tissue and cell in the body. That is why sufficient concentrations of serum 25(OH)D are essential for optimal functioning of these tissues and cells.

The major function of vitamin D compounds is to enhance the active absorption of ingested calcium (and phosphate). This assists in building bone at younger ages and ensures that, despite obligatory urinary losses, bone does not need to be desorbed to maintain blood calcium concentrations.

Moreover, sufficient concentrations of vitamin D may be important in reducing the occurrence of autoimmune diseases, such as multiple sclerosis, rheumatoid arthritis, diabetes, and some cancers. Adequate vitamin D may also allow for a normal innate immune response to pathogens, improve cardiovascular function and mortality and increase insulin responsiveness.

A century since the discovery of its dual origin, many questions have been raised and remain unanswered about vitamin D’s concentrations in human beings. For example, why is vitamin D so important? Why should we be concerned about vitamin D deficiency during pregnancy? What concentrations of the vitamin are optimal in adults and children? Do these optimal concentrations vary for the prevention of various disorders or in differing human populations? What amount of supplementation or sunlight exposure is needed to achieve and maintain these concentrations? And how much vitamin D can we really take safely?

Luckily, in the last few years, numerous clinical studies, including crucial randomised controlled trials (RCTs) of vitamin D supplementation were conducted in the search for answers to the above mentioned questions and more. Successful completion of experimental trials was essential to obtain valuable information on the effect of vitamin D in preventing a wide range of disorders, and also for establishing the efficacy and safety of vitamin D supplementation.
literature. The panel reached substantial agreement about the need for vitamin D supplementation in adult patients with, or at risk for fractures, falls, cardiovascular or autoimmune diseases, and cancer. A target range of at least 75 to 100 nmol/L was recommended.53

However, one study of a convenience sample of 93 healthy young adults recruited from the University of Hawaii and a Honolulu skateboard shop questioned the frequently suggested serum 25(OH)D sufficiency cutoff of 75 nmol/L. The investigators recruited these prototypic "surfer dudes" (mean age: 24 years; mean body mass index [BMI], in kg/m²: 23.6). On the basis of a self-reported minimum outdoor sun exposure of 15 hours (mean: 29 hours) per week during the preceding 3 months; 40% reported never using sunscreen, and the group overall reported an average of 22.4 hours per week of unprotected sun exposure. All were clinically tanned. Nevertheless, the group’s mean 25(OH)D concentration was 79 nmol/L, and 51% had a concentration below the suggested 75 nmol/L cutoff for sufficiency. The study group was multiracial, but even among the 37 white subjects, the mean value was only 92.8 nmol/L and the highest value was 155 nmol/L.63

On the other hand, Luxwolda et al. measured the sum of serum 25-hydroxyvitamin D2 and D3 (25(OH)D) concentrations of thirty-five pastoral Maasai (mean age: 34 ± 10 years, 43% male) and twenty-five Hadzabe hunter-gatherers (mean age: 35 ± 12 years, 84% male) living in Tanzania. They had skin type VI, wore a moderate degree of clothing, spent the majority of the day outdoors, but avoided direct exposure to sunlight when possible. The mean serum 25(OH)D concentrations of Maasai and Hadzabe were 119 (range 58–167) and 109 (range 71–171) nmol/L, respectively. These concentrations were not related to age, sex, or BMI.64 These recent data suggest that a public health goal of ≥75 nmol/L, or even ≥100 nmol/L, for the entire population can be achieved by sun exposure.

How much Vitamin D is required to Optimise Bone and Global Health?

In 2011, the IOM released revised recommendations for the daily intake of vitamin D based on the body’s need for skeletal health.9 The recommended dietary

the production of proinflammatory cytokines.35,54 Maternal nutritional vitamin D status has a good effect on childhood bone mineral accrual and is important also for fetal “imprinting” that may affect neurodevelopment, immune function, and chronic disease susceptibility later in life, as well as soon after birth.55,56

Also, maternal vitamin D insufficiency during pregnancy is significantly associated with offspring language impairment. Maternal vitamin D supplementation during pregnancy may reduce the risk of developmental language difficulties among children.57 Meanwhile, substandard vitamin D intake during pregnancy may lead to decreased birth weight.58 Moreover, maternal vitamin D deficiency in early pregnancy may be an independent risk factor for preeclampsia59 and may be associated with increased odds of primary caesarean section.60 Merewood et al. found that 28% of women with serum 25(OH)D concentrations less than or equal to 37.5 nmol/L had a caesarean section, compared with only 14% of women with higher 25(OH)D concentrations (≥37.5 nmol/L).60

What is the “Normal” Circulating 25(OH)D Concentration in Human Beings?

Vitamin D deficiency has been historically defined and recently recommended by the Institute of Medicine (IOM), USA, as a 25(OH)D concentration of less than 50 nmol/L. Vitamin D insufficiency has been defined as a 25(OH)D concentration of 50–75 nmol/L.61 Vitamin D deficiency can be further classified as mild (25–50 nmol/L), moderate (12.5–25.0 nmol/L), and severe (<12.5 nmol/L).5 However, the preponderance of evidence points to optimal serum 25(OH)D concentrations of at least 80 nmol/L to maximise vitamin D’s effect on calcium, bone, and muscle metabolism.1,3,5,62 Based on a quick review of the literature for vitamin D during pregnancy, as well as a more detailed review for other diseases, Grant found that serum 25(OH)D concentrations above 75–100 nmol/L are required for good pregnancy outcomes, fetal health, and optimal health in general.35 Similarly, an international expert panel formulated recommendations on vitamin D for clinical practice, taking into consideration the best recent evidence available based on published
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received 400, 2,000 or 4,000 IU vitamin D₃ per day until delivery. The relative risk (RR) for achieving ≥80 nmol/L within one month of delivery was significantly different between 2,000 and 400 IU. Circulating 25(OH)D had a direct influence on circulating 1,25(OH)₂ D concentrations throughout pregnancy with maximal production of 1,25(OH)₂ D in all strata in the 4,000 IU group. There were no differences between groups on any safety measure. Not a single adverse event was attributed to vitamin D supplementation or circulating 25(OH)D concentrations. Another study by Hollis was conducted in Columbia, South Carolina, USA. The study included diverse groups of women who were randomised to 2,000 or 4,000 IU vitamin D₃/day irrespective of baseline 25(OH)D at <16 weeks’ gestation. The aim was to confirm the NIH/NICHD study findings and to prove that no adverse events are associated with vitamin D supplementation. Both of these studies proved that vitamin D supplementation with 4,000 IU vitamin D/day for pregnant women was safe and effective in achieving vitamin D sufficiency in a racially diverse group. In both studies, higher maternal circulating 25(OH)D was associated with a lower risk of co-morbidities of pregnancy.

What are the Possible Effects on Health of High Concentrations of Vitamin D?

According to Heaney, an intake of 1,000 IU vitamin D/day results in an increase of approximately 25 nmol/L in 25(OH)D, although individual responses vary. Accordingly, most international authorities consider a vitamin D intake of 2,000 IU/day as absolutely safe, although literature review revealed that even doses of up to 10,000 IU/day supplemented over several months did not lead to any adverse events.

In 2011, the IOM re-evaluated the potential for high intakes of vitamin D to produce adverse effects and set a safe tolerable upper intake level (UL) for vitamin D of 4,000 IU/day for ages 9 and older and lower for infants (0–6 months: 1,000 IU/day; 6–12 months: 1500 IU/day) and younger children (1–3 years: 2,500 IU/day; 4–8 years: 3,000 IU/day). According to Ross et al., the starting point for the announced UL for vitamin D was 10,000 IU/day.

allowances (RDAs) for vitamin D are 600 IU/d for ages 1–70 years and 800 IU/d for ages 71 years and older, corresponding to a serum-25-hydroxyvitamin D concentration of at least 50 nmol/L. RDAs for vitamin D were based on conditions of minimal sun exposure due to wide variability in vitamin D synthesis from UV light and the risks of skin cancer.

The recommendations of the American Academy of Pediatrics (AAP) are 400 IU/day of vitamin D for exclusively and partially breastfed infants shortly after birth, to be continued until they are weaned and consume ≥1,000 mL/day of vitamin D-fortified formula or whole milk. Similarly, all non-breastfed infants ingesting <1,000 mL/day of vitamin D-fortified formula or milk should receive a vitamin D supplement of 400 IU/day. The AAP also recommends that older children and adolescents who do not obtain 400 IU/day through vitamin D-fortified milk and foods should take a 400 IU vitamin D supplement daily. However, this latter recommendation, issued in November 2008, is less than the Food and Nutrition Board’s vitamin D RDA of 600 IU/day for children and adolescents that was issued in November 2010.

All these recommendations have stimulated considerable debate. Many scientists thought that to increase nutritional vitamin D to meaningful concentrations, dietary intakes of ≥2,000 IU/day may be required. In order to calculate the needs of a human body, one should know that sunlight exposure sufficient to result in a mild sunburn for a Caucasian adult in a bathing suit raises the serum 25(OH)D to a concentration comparable to that of a person taking 10,000 to 20,000 IU of vitamin D₂ orally; which could be the daily requirement for human beings. Thus, raising the blood concentration of 25(OH)D consistently above 75 nmol/L may require at least 1,000–2,000 IU/day of supplemental vitamin D. Higher concentrations of 2,000 IU/day for children 0–1 years, 4,000 IU/day for children 1–18 years, and 10,000 IU/day for children and adults 19 years and older may be needed to correct vitamin D deficiency.

To end the debate, Bruce Hollis et al. have recently conducted a randomised controlled trial, the National Institutes of Health/National Institute of Child Health & Human Development (NIH/NICHD) study, in which women with a singleton pregnancy at 12–16 weeks’ gestation
Given that toxicity is not the appropriate basis for a UL that is intended to reflect long-term chronic intake and to be used for public health purposes, this value was corrected for uncertainty based on chronic disease outcomes and all-cause mortality to 4,000 IU/day. However, Garland and colleagues pointed out that the supplemental dose, ensuring that 97.5% of the population study achieved a serum 25(OH)D of at least 100 nmol/L, was 9,600 IU/day.

It should be mentioned here that sunbathing can produce vitamin D doses equivalent to an oral vitamin D intake of up to 20,000 IU/day and in healthy subjects who spent prolonged periods in a sunny environment, measured 25(OH) D concentrations rarely exceed 250 nmol/L, suggesting that this level may be considered a safe upper limit for serum 25(OH)D levels. Furthermore, a benefit-risk assessment of vitamin D supplementation conducted by Bischoff-Ferrari et al. reported that hypercalcæmia caused by excess vitamin D in generally healthy adults was observed only if daily intake was >100,000 IU or if the 25(OH) D level exceeded 250 nmol/L. Accordingly, they pointed out that 250 nmol/L should be considered a safe limit, but not as an upper limit to target in clinical practice. Similarly, Hathcock et al., noting the absence of toxicity in clinical trials conducted in healthy adults that used vitamin D doses of ≥10,000 IU, supported the confident selection of this value as the UL.

Conclusion

Over the past two decades, scientists, clinicians and researchers have generated a strong body of evidence to address the problem of vitamin D deficiency and provide advice for correcting its status among all ages, genders and racial/ethnic groups. Many studies, some randomised and some not, have suggested that a population with a higher vitamin D intake would be healthier overall. Accordingly, the following can be recommended.

First, vitamin D can be obtained from production by the skin after brief UV exposure. Exposure to bright midday sunlight, rich in UVB wavelengths, is a very efficient way to make vitamin D. Unfortunately, the action spectrum for vitamin D photosynthesis is essentially identical to the spectrum that damages DNA and causes skin cancer. The study done by Samanek et al. in 2006 illustrates the complexities of calculating UV exposure times and clearly indicates that it is impractical to generate a simple nationally uniform message that prescribes minutes of sun exposure to the general population, given the number of variables that need to be taken into consideration. In response to potential confusion over mixed messages about the risks and benefits of sun exposure, a collaboration of the Cancer Council Australia, the Australian and New Zealand Bone and Mineral Society, Osteoporosis Australia and the Australasian College of Dermatologists gathered Australian experts in Melbourne in December 2006, to review the latest evidence on vitamin D and develop a position statement. Those experts suggested that people should continue to protect themselves from overexposure, especially during peak ultraviolet radiation periods (10 am to 3 pm). For most people, sun protection to prevent skin cancer is required when the UV index is moderate or above (i.e. UV index is 3 or higher). At such times, sensible sun protection behaviour is warranted and is unlikely to put people at risk of vitamin D deficiency. Most people probably achieve adequate vitamin D concentrations through the UVB exposure they receive during typical day-to-day outdoor activities. For example, fair skinned people can achieve adequate vitamin D concentrations (>50 nmol/L) in summer by exposing the face, arms and hands or the equivalent area of skin to a few minutes of sunlight on either side of the peak UV periods on most days of the week. In winter, when UV radiation concentrations are less intense, maintenance of vitamin D concentrations may require 2–3 hours of sunlight exposure to the face, arms and hands or equivalent area of skin over a week.

Second, some groups in the community are at increased risk of vitamin D deficiency. They include naturally dark-skinned people, those who cover their skin for religious or cultural reasons, the elderly, infants of vitamin D deficient mothers, and people who are housebound or are in institutional care. Naturally dark-skinned people (Fitzpatrick skin type 5 and 6) are relatively protected from skin cancer by the pigment in their skin; they could therefore safely increase their sun exposure. Others on this list should discuss their vitamin D status with their medical practitioner as some might benefit from dietary supplementation with vitamin D.
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Both the USA and Canada mandate the fortification of infant formula with vitamin D: 40–100 IU/100 kcal in the USA, and 40–80 IU/100 kcal in Canada. Sixth, in supplements and fortified foods, vitamin D is available in two forms, D$_2$ (ergocalciferol) and D$_3$ (cholecalciferol), which differ chemically only in their side-chain structure. However, Vitamin D$_3$ is approximately 87% more potent in raising and maintaining serum 25(OH)D concentrations and produces 2- to 3-fold greater storage of vitamin D than does vitamin D$_2$. Accordingly, vitamin D$_3$ should be the preferred treatment option when correcting vitamin D deficiency through supplementation using an intermittent regimen. However, when given as daily doses, vitamin D$_2$ and D$_3$ seem to have similar effects on 25(OH)D levels. Seventh, the use of UVB irradiance may be useful in certain cases. Solar UVB radiation with a wavelength of 290–320 nanometers penetrates uncovered skin and converts cutaneous 7-dehydrocholesterol to previtamin D$_3$, which in turn becomes vitamin D$_3$. However, the most commonly used lamps do a poor job of simulating the UVB light intensity of natural sunlight. The only lamps that come close to the intensity of natural sunlight are “sunlamps”, which are sometimes used to treat psoriasis. The moderate use of commercial tanning beds that emit 2–6% UVB radiation is also effective. Eighth, in practice, testing for 25(OH)D is recommended after at least 3 months of supplementation (usually 6–12 months). Currently, 25(OH)D measurement is reasonable in groups of people at high risk for vitamin D deficiency and in whom a prompt response to optimisation of vitamin D status is expected. However, serum 25(OH)D assays are expensive, and the need for universal screening has not yet been proven.

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There has been an increase in the number of near-term and term infants reported with acute bilirubin encephalopathy, which has resulted in an increase in the number of readmissions of infants to hospitals. This can partially be attributed to shorter postpartum hospital stays, and limited post-natal follow-up. To prevent kernicterus, clinicians need to understand the physiology of bilirubin production and excretion, and develop a systematic approach to the causes and management of neonatal icterus. This issue is highlighted here with specific relation to near-term and term newborns.

**Epidemiology**

Nearly all newborn infants have a total serum bilirubin (TSB) value greater than 1 mg/dL (17.1 µmol/L), which is at the upper limit of normal for an adult. Most newborns appear clinically jaundiced.

In nearly all newborn infants, the yellow discoloration of the skin and/or sclerae of newborn infants caused by tissue deposition of bilirubin. Physiological jaundice is mild, unconjugated (indirect-reacting) bilirubinaemia, and affects nearly all newborns. Physiological jaundice levels typically peak at 5 to 6 mg/dL (86 to 103 µmol/L) at 72 to 96 hours of age, and do not exceed 17 to 18 mg/dL (291–308 µmol/L). Levels may not peak until seven days of age in Asian infants, or in infants born at 35 to 37 weeks’ gestation. Higher levels of unconjugated hyperbilirubinaemia are considered pathological and occur in a variety of conditions. The clinical features and management of unconjugated hyperbilirubinaemia in healthy near-term and term infants, as well as bilirubin toxicity and the prevention of kernicterus, are reviewed here. The pathogenesis and aetiology of this disorder are discussed separately.

**Keywords:** Newborn; Icterus; Hyperbilirubinaemia; Jaundice.
Pathologic hyperbilirubinaemia occurs when the TSB exceeds the hour-specific 95th percentile using the published nomogram in Figure 1. The nomogram was developed for a racially diverse population in Philadelphia in which nearly 60% were breastfed. Infants were excluded if they had haemolytic conditions or required phototherapy before 60 hours to control rapidly rising TSB levels. However, rates of hyperbilirubinaemia vary substantially between centres because of racial differences, haemolytic conditions, and breastfeeding practices. In a multinational study, the proportion of infants with TSB levels at or above the 95th percentile at 30 hours ranged from approximately 5% in Hong Kong and China, to 40% in Kobe, Japan.

Clinical Features

Risk factors for the development of jaundice in near-term infants were obtained from clinical histories. They included gestational age of 35 to 37 weeks; polycythaemia; assisted deliveries through such methods as vacuum or forceps instrumentation; trauma during labour or delivery; maternal diabetes; Asian race; blood group incompatibility; poor breastfeeding practices, or a previous sibling with jaundice.

Visual inspection of skin colour can be used to detect jaundice, but it is not a reliable method to assess the level of bilirubin or identify infants at risk for rapidly rising bilirubin levels, especially in those with dark skin. The examination should be performed with adequate ambient light. Pressing on the skin with a finger reduces local skin perfusion and may facilitate detection of jaundice.

Jaundice progresses in a cephalocaudal direction. The face and sclera typically appear icteric when bilirubin levels reach 6 to 8 mg/dL (103 to 137 µmol/L), whereas the entire body, including palms and soles, appears jaundiced at values of 12 to 13 mg/dL (205 to 222 µmol/L). TSB or transcutaneous bilirubin (TcB) levels should be measured in an infant with jaundice detected below the umbilicus.

Physical examination may identify signs that suggest risk for pathological jaundice. They include pallor, enclosed haemorrhage such as cephalhaematoma, and bruising.
The TSB concentration is compared to an hour-specific percentile-based nomogram. TSB levels in a term newborn typically peak at 5 to 6 mg/dL (86 to 103 µmol/L) at 72 to 96 hours of age, and do not exceed 17 to 18 mg/dL (291-308 µmol/L). The peak may not be reached until seven days of age in Asian infants, or in infants born at 35 to 37 weeks’ gestation.

Infants with hour-specific values that are greater than or equal to the 95th percentile are at increased risk for the development of clinically significant hyperbilirubinaemia, requiring intervention. In a racially diverse population with a 60% rate of breastfeeding, 95th percentile values for TSB were approximately 8, 10, 12, and 16 mg/dL (137, 171, 205, and 274 µmol/L) at 24, 36, 48, and 72 hours, respectively.

Infants who have TSB values greater than or equal to the 95th percentile, or who are suspected of having haemolytic disease, require subsequent measurement of TSB levels and further evaluation to determine the aetiology of their jaundice. Initial tests that should be obtained are blood type and direct anti-globulin tests, a complete blood count and smear, and a reticulocyte count. The mother’s blood type and antibody status usually are known from the prenatal history. If an infant is of Asian origin and the TSB concentration is ≥18 mg/dL (222 µmol/L), glucose-6-phosphate dehydrogenase (G6PD) should be measured. However, G6PD measurements are not universally available, and the results usually are not timely enough to affect clinical decisions.

End-tidal measurement of carbon monoxide (CO) corrected for ambient CO (ETCOc) provides a noninvasive assessment of bilirubin production because catabolism of heme results in equimolar quantities of bilirubin and CO. Elevated ETCOc values (>2.0 parts per million) can identify infants with increased bilirubin production (most often caused by haemolysis) who require additional evaluation or close monitoring. In one study, the ETCOc value at 30 hours of age exceeded the mean value (1.48 ppm) in 76% of hyperbilirubinaemic infants.

Kernicterus

Bilirubin is a potential neurotoxin. Unconjugated bilirubin that is not bound to albumin (free bilirubin) can enter the brain and cause focal necrosis of the neurons and glia, resulting in bilirubin encephalopathy, which is also known as kernicterus. The regions most often affected include the basal ganglia and the brain stem nuclei for oculomotor and auditory function, accounting for the clinical features of this condition.

Near-term and term infants are at risk for kernicterus when TSB concentrations exceed 25 to 30 mg/dL (428 to 513 µmol/L). However, the relationship between TSB and kernicterus is variable and influenced by other factors such as bilirubin affinity for albumin, which is reduced in premature and sick infants. Most unconjugated bilirubin is normally bound to albumin, resulting in low levels of free bilirubin. High TSB concentrations may exceed the capacity of albumin to bind bilirubin and lead to higher levels of free bilirubin, which may be neurotoxic. Although measurement of free bilirubin concentration would be useful to guide therapy, clinical testing is not universally available.

Drugs such as sulfisoxazole, moxalactam, and ceftriaxone can displace bilirubin from albumin and increase the risk of kernicterus. Acidosis increases movement of bilirubin into tissues and, thus, can contribute to the development of kernicterus.

Kernicterus can occur in healthy term infants. However, infants at increased risk are those who are near term (35 to 37 weeks), breastfed, have haemolytic disease, and are discharged home before 48 hours. To minimise the risk of bilirubin encephalopathy, these infants require close surveillance because the peak TSB levels will be reached after discharge.

Laboratory Evaluation

TSB and the direct-reacting serum bilirubin concentration are measured in infants with jaundice. If the direct-reacting bilirubin is greater than 1.5 to 2.0 mg/dL (26 to 34 µmol/L), causes of cholestatic jaundice should be investigated. The following discussion applies to healthy term and near-term infants with hyperbilirubinaemia. Infants who appear ill or are premature require more extensive evaluation.
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Transcutaneous devices that use multi-wavelength spectral reflectance can be used to estimate TSB in order to avoid blood sampling. In contrast to older devices, this method is not affected by skin pigmentation. In one report of a racially and ethnically diverse group of 490 newborns, a close correlation was found between transcutaneous and TSB measurements.

Prevention of Severe Hyperbilirubinaemia
Infants with severe hyperbilirubinaemia are at risk for developing kernicterus, although only a small number will do so (see section on kernicterus above). Timely identification and treatment of infants with severe hyperbilirubinaemia will prevent most cases of kernicterus. Infants at risk require close surveillance and follow-up.

Term and near-term infants should be evaluated for jaundice between 72 and 96 hours of age, the time at which TSB levels typically peak. However, many infants are discharged from the hospital prior to 48 hours of age; these infants should be examined for jaundice by a clinician within one to two days of discharge.

TSB levels are often higher in breastfed than in formula-fed infants. In addition, milk intake may be inadequate until lactation is well established, resulting in volume depletion and weight loss. Increased surveillance is needed for infants born at 35 to 37 weeks’ gestation because they are at increased risk for early difficulty with breastfeeding.

Counselling regarding jaundice and breastfeeding should be provided before discharge where the importance of frequent feedings should be emphasised. Lactation consultants and home visits by a nurse may be helpful. Until lactation is well-established in significantly jaundiced infants, it may be helpful to interrupt breast feeding briefly and supplement with formula for a short period (supplementation with water is not recommended).

A root cause analysis of factors contributing to cases of kernicterus identified potentially correctable causes. These include: 1) discharge within 48 hours of birth with no follow-up within 48 hours of discharge; 2) failure to measure the bilirubin concentrations in an infant with jaundice within 24 hours of birth; 3) failure to recognise risk factors for hyperbilirubinaemia; 4) lack of concern regarding the presence of jaundice; 5) delayed measurement of TSB in infants with severe jaundice; 6) delayed initiation of phototherapy in infants with elevated TSB levels, and 7) lack of response to parental concerns regarding jaundice, lethargy, or poor feeding.

Prediction of Severe Hyperbilirubinaemia
A percentile-based nomogram, such as that in Figure 1, can be used to predict the subsequent risk for severe hyperbilirubinaemia. In another report, the combined use of an hour-specific TSB measurement and ETCOc did not improve the predictive ability of an hour-specific TSB alone. However, these clinical devices are not currently available. In this study, in contrast to the report on which the nomogram was based that used TSB alone, 4 of 620 infants with TSB levels in the low risk zone (<40th percentile) at 30 ± 6 hours subsequently developed TSB levels greater or equal to those in the 95th percentile. This finding supports the need for early follow-up of all infants regardless of their risk zone at discharge.

Universal Screening
Universal screening of infants for TSB levels prior to discharge has been proposed to facilitate identification of infants at high risk for the development of severe hyperbilirubinaemia. Limitations of this approach are the need for blood sampling and the cost of TSB measurement. Use of transcutaneous methods for screening may decrease the need for phlebotomy, and reduce costs. An alternative approach is clinical assessment of jaundice before and within one to two days of discharge, and subsequent TSB measurement in jaundiced infants.

Treatments
Phototherapy is the standard treatment for pathologic unconjugated hyperbilirubinaemia. Rare cases of extremely high TSB levels (>25 mg/dl) require an exchange transfusion.
PHOTOTHERAPY

Phototherapy consists of exposing the infant’s skin to blue-to-green light in wavelengths ranging from 400–520 nm. It is a safe and efficient method to reduce the toxicity of bilirubin and increase its elimination. Phototherapy detoxifies bilirubin by three mechanisms: structural isomerisation to lumirubin, photoisomerisation to a less toxic isomer, and photooxidation to polar small molecules. These processes are thought to occur in the blood vessels or interstitial spaces of the skin.

Phototherapy with blue light phototherapy converts bilirubin into lumirubin in a process of structural isomerisation that is not reversible. Lumirubin, a more soluble substance than bilirubin, is excreted without conjugation into bile and urine. It is the principal mechanism by which phototherapy reduces the TSB concentration. Phototherapy with blue light phototherapy also converts the stable 4Z, 15Z bilirubin isomer to the 4Z, 15E isomer, which is more polar and less toxic than the common form. Like lumirubin, it is excreted into bile without conjugation. Unlike structural isomerisation to lumirubin, photoisomerisation is reversible, and some of the 4Z, 15E isomer in the bile is converted back into the stable 4Z, 15Z isomer. Photoisomerisation is the second important mechanism to increase bilirubin excretion. TSB photo oxidation reactions convert bilirubin to colourless, polar compounds that are excreted primarily in the urine. This mechanism accounts for a small proportion of bilirubin elimination.

The dose of phototherapy, known as irradiance, times duration determines its efficacy. Irradiance depends upon the intensity of the blue light, its distance from the infant, and the surface area exposed. It usually is expressed for a certain wavelength band (spectral irradiance). Fluorescent blue light typically is used at a dose of approximately 30 µW/cm²/nm of area exposed. Blue lights are more effective at reducing bilirubin but may interfere with the detection of cyanosis. The use of white daylight fluorescent lights/lamps is better than no phototherapy.

Fluorescent lights are placed 15 to 20 cm above the infant. We use light banks with eight alternating white and blue fluorescent bulbs. This combination increases the irradiance but lessens the eye strain for clinicians. Halogen white light lamps are hot and can cause thermal injury. They should be placed at the manufacturer recommended distance from the patient.

Fibre optic blankets generate little heat and can be placed close to the infant and provide higher irradiance than do fluorescent lights. However, blankets are small and rarely cover sufficient surface area to be effective when used alone in near-term and term infants. They can be used as an adjunct to overhead fluorescent or halogen lights. High intensity gallium nitride light emitting diodes (LEDs), such as neoblue, are as effective as conventional fluorescent light phototherapy.

For intensive phototherapy (30 µW/cm²/nm) of infants with TSB levels greater than 25 mg/dL (428 µmol/L), a bank of special blue lights should be placed 10 to 12 cm from the infant’s body to expose the maximum surface area to light. Premature and hypothermic babies should be placed in an open crib or on a warmer. The area covered by the diaper should be minimised and the infant’s eyes should be shielded with a blindfold with care taken so that the blindfold does not cover the nose.

Temperature, time of exposure, irradiance (if possible), and the infant’s hydration status should all be monitored. Infants should continue oral feedings by breast or bottle. Intravenous hydration is needed only in cases of significant volume depletion. Phototherapy should be continuous, with interruptions only for feeding. If the TSB is at a near toxic level, fibre optic blanket exposure can continue during the feedings.

The following discussion applies to healthy term and near-term infants. Infants who appear ill or are premature require more aggressive intervention. For healthy term and near-term infants, we initiate phototherapy according to the 2004 practice and parameter recommendations of the American Academy of Pediatrics (AAP) on the management of hyperbilirubinaemia. Phototherapy is started if TSB levels are 15, 18, or 20 mg/dL (257, 308, and 342 µmol/L) at 25 to 48, 49 to 72, or >72 hours after birth, respectively. These values exceed the 95th percentile for hour-specific TSB concentrations, predicting increased risk for developing severe hyperbilirubinaemia after discharge. For this reason, clinicians often initiate treatment for TSB levels that are 2 to 3 mg/dL (34–51 µmol/L) lower than the above values, especially for near term infants (35–37 weeks), or infants with other risk factors.
Infants with clinical jaundice within the first 24 hours of birth frequently have haemolysis. They require immediate evaluation and close surveillance to assess the need for phototherapy. In infants with other causes of increased bilirubin production, such as cephalohaematoma or extensive bruising, or in infants suspected of having conjugation disorders, we start phototherapy when the hour-specific TSB concentration is in a high intermediate risk zone (>75th percentile).

When TSB values are ≥20 mg/dL (342 µmol/L), the measurement should be repeated four to six hours after phototherapy is initiated to assess the response. For lower initial values, TSB should be measured after 24 hours and then once daily while phototherapy continues. However, measurement of serum bilirubin will also depend on the aetiology of the jaundice, rate of rise, etc., and may be indicated more often even when levels are not yet at 20 mg/dL. A decrease in TSB level can be measured as soon as two hours after initiation of treatment. Intensive phototherapy should result in a decline of TSB of at least 1 to 2 mg/dL (17–34 µmol/L) within four to six hours.2

Our centre discontinues phototherapy when the hour-specific TSB level falls to a value less than the 95th percentile, or has decreased 4 to 5 mg/dL (68–86 µmol/L) when measured 18 to 24 hours later. Although the value following discontinuation is known as the rebound bilirubin, typically it is lower than the previous TSB during treatment. In one study of 161 infants with birth weights of more than 1800 grams, the rebound TSB was significantly lower 17 hours after termination of phototherapy (11.5 versus 12.2 mg/dL, 197 versus 209 µmol/L).21

Exchange transfusion is used to remove bilirubin from the circulation when intensive phototherapy fails. It is especially useful for infants with increased bilirubin production from immune-mediated haemolysis because the circulating antibodies and the sensitised red blood cells also are removed.

An exchange transfusion is performed when severe hyperbilirubinaemia does not respond to intensive phototherapy. According to the AAP practice parameters, an exchange transfusion is indicated in healthy near-term and term infants when TSB levels are greater than or equal to 20 mg/dL (342 µmol/L) at 24 to 48 hours of age, or are at or greater than 25 mg/dL (428 µmol/L) thereafter. Failure of intensive phototherapy occurs if TSB levels do not decrease by 1 to 2 mg/dL (17–34 µmol/L) within four to six hours of initiation of phototherapy. An exchange transfusion also should be performed in infants with high TSB levels as per the nomogram, and in any infant with any signs of bilirubin neurotoxicity.

Exchange transfusion is indicated in cases of haemolysis, especially immune-mediated, if the anaemia is severe and resulting in hydrops, or the TSB is rising rapidly and is expected to reach 25 mg/dL (428 µmol/L) within 48 hours. Exchange transfusions will correct the anaemia without causing circulatory overload and remove maternal antibodies and sensitised erythrocytes. Less severely affected patients can be managed with intensive phototherapy to reduce TSB levels, and transfusions of packed red blood cells to correct the anaemia.

A double-volume exchange transfusion removes approximately twice the infant’s circulating blood volume (blood volume is approximately 80 to 90 mL/kg), replacing it with appropriately cross-matched fresh or reconstituted (from packed red blood cells and fresh frozen plasma) whole blood. The procedure involves placement of a central catheter and the subsequent removal and replacement of the maximum amount of blood that should be withdrawn at any one time (approximately 5 ml per Kg body weight). Most of the bilirubin is extravascular; as a result, an exchange transfusion removes approximately 25% of the total body bilirubin.21 An infusion of albumin (1 g/kg) one to two hours before the procedure moves more extravascular bilirubin into the infant’s circulation, allowing removal of more bilirubin.21

After the procedure, TSB levels typically fall to approximately half of the pre-exchange value, and
then increases to approximately two-thirds of that level as the extravascular and vascular bilirubin re-equilibrate. A double volume exchange transfusion replaces approximately 85% of the infant’s red blood cells.

The risks of exchange transfusions result from the use of blood products and from the procedure itself. Possible complications include blood-borne infection, thrombocytopenia, coagulopathy, graft-versus-host disease, necrotising enterocolitis, portal vein thrombosis, electrolyte abnormalities, cardiac arrhythmias, and sudden death.24 Most complications occur in sick infants and are rare in healthy infants. In a retrospective review of 15 years of experience at two academic medical centres, one of 81 healthy infants developed necrotising enterocolitis after exchange transfusion, and none died.22

Pharmacological Agents
Pharmacological agents, including intravenous immunoglobulin (IVIG), phenobarbital, and metalloporphyrins can be used to inhibit haemolysis, increase conjugation and excretion of bilirubin, or inhibit the formation of bilirubin. However, IVIG is currently used only to treat unconjugated hyperbilirubinaemia.

INTRAVENOUS IMMUNOGLOBULIN
Intravenous immunoglobulin IVIG (500 mg/kg per dose IV over two hours) may reduce the need for exchange transfusions in infants with haemolytic disease caused by Rh or ABO incompatibility.23 The mechanism is uncertain, but IVIG is thought to inhibit haemolysis by blocking antibody receptors on red blood cells.

PHENOBARBITAL
Phenobarbital increases the conjugation and excretion of bilirubin and decreases postnatal TSB levels when given to pregnant women or infants; however, prenatal administration of phenobarbital may adversely affect cognitive development and reproduction.24 As a result, phenobarbital is not used to treat indirect hyperbilirubinaemia. There are exceptional circumstances, like prolonged jaundice in Gilbert’s syndrome, where it might be useful.

METALLOPORPHYRINS
Synthetic metalloporphyrins, such as tin mesoporphyrin (SnMP), reduce bilirubin production by competitive inhibition of heme oxygenase.25 In one report, for example, term and near-term infants with G6PD deficiency given SnMP at approximately 27 hours of age had lower and earlier peak TSB values than did control infants with and without G6PD deficiency.11 No treated infant required phototherapy, compared to 31% and 15% in the controls with and without G6PD deficiency, respectively. However, metalloporphyrins are not available for clinical use.

Conclusion
The following recommendations only apply to healthy term and near-term infants. Infants who appear ill, are premature, or have evidence of haemolysis require more intensive evaluation and management.

Infants should be assessed for jaundice at 24 to 48 hours of age and prior to hospital discharge. Measurement of serum or transcutaneous bilirubin concentration is preferred. Alternatively, the infant can be assessed by visual inspection and a measurement of TSB levels should be obtained in those who appear jaundiced.

TSB values should be compared to an hour-specific nomogram to predict the risk of subsequent development of clinically significant hyperbilirubinaemia. Infants at high risk require increased surveillance.

Infants discharged within 48 hours of birth require a follow-up evaluation within 24 to 48 hours of discharge. Infants at high risk for the development of significant hyperbilirubinaemia should be evaluated within 24 hours of discharge. In addition, parents should also be told to return immediately if the infant becomes visibly more jaundiced or develops any sort of neurological symptom.

Lactation counselling should be provided for breastfeeding mothers. Near-term (35 to 37 weeks) infants are at greater risk of receiving inadequate fluid and nutrition, and require increased surveillance.
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References


Snoring-Induced Nerve Lesions in the Upper Airway

*Rajesh P Poothrikovil and Mohammed A Al Abri

The prevalence of habitual snoring is extremely high in the general population, and is reported to be roughly 40% in men and 20% in women. The low-frequency vibrations of snoring may cause physical trauma and, more specifically, peripheral nerve injuries, just as jobs which require workers to use vibrating tools over the course of many years result in local nerve lesions in the hands. Histopathological analysis of upper airway (UA) muscles has shown strong evidence of a varying severity of neurological lesions in groups of snoring patients. Neurophysiological assessment shows evidence of active and chronic denervation and re-innervation in the palatopharyngeal muscles of obstructive sleep apnoea (OSA) patients. Neurogenic lesions of UA muscles induced by vibration trauma impair the reflex dilation abilities of the UA, leading to an increase in the possibility of UA obstruction. In a person with OSAS, the UA muscles relax excessively during sleep. This allows intermittent cessation of breathing due to UA obstruction. In a person with OSAS, the UA muscles relax excessively during sleep. This allows intermittent cessation of breathing due to obstruction.

**Keywords:** Neurogenic; Obstructive sleep apnoea syndrome (OSAS); Palatopharyngeal Muscle; Snoring; Upper airway; Trauma.

The American Academy of Sleep Medicine (AASM) defines snoring as a sound originating from the upper airway (UA) that does not occur with apnoea or hyperventilation, and that is caused by vibrations of different tissues in the pharynx. A person who snores for more than 10–20% of a monitored night, or more than 3 or 4 nights a week is classified as a habitual snorer. An association between snoring and obstructive sleep apnoea syndrome (OSAS) was first observed in 1975. OSAS is considered a progressive disorder that starts, often early in life, with habitual snoring. Based on different epidemiological studies performed between 1980 and 2007, the mean prevalence of snoring in the general population is approximately 32% in men and 21% in women; however, the prevalence of obstructive sleep apnoea (OSA) is 4% in men and 2% in women. OSAS involves the intermittent cessation of breathing due to obstruction. In a person with OSAS, the UA muscles relax excessively during sleep. This allows tissues (e.g. tonsils and adenoids) supported by the...
Snoring-Induced Nerve Lesions in the Upper Airway

patients than in non-obese controls. Sleep disordered breathing (SDB) results from an imbalance between negative pharyngeal pressure and the opposing force of the UA muscles. Abnormal function of the UA, such as sleep-related suppression of UA muscle activity and a decrease in UA dilator muscle force are thought to be the main source of obstructions and symptoms in the OSAS.15,16 Phasic activation of the muscles of the nose, pharynx and larynx has been shown to occur before diaphragm and intercostal muscle activity, suggesting a pre-activation of the UA muscles in preparation for the development of negative pressure.17,18 The UA is rich in neural receptors which is a key factor of tonic genioglossus electromyogram (EMG) activity. During inspiration, the UA dilatory muscles, the genioglossus and geniohyoid contract, or shorten, their muscle fibres through an increase in EMG activity. These inspiration-related muscle activations result in the enlargement of the UA.19 Loss of genioglossus EMG tone may lead to an increase in pharyngeal resistance.20 In order to compensate for abnormal anatomy and/or a more collapsible pharyngeal airway, OSAS patients display augmented genioglossus muscle activity during wakefulness as compared with healthy subjects.21 This reflex compensatory neuromuscular mechanism is lost at sleep onset (loss of awake compensation) in both the control and in OSAS patients, but is associated with pharyngeal collapse under conditions of chronic airway loading.22 When the tongue moves posteriorly due to a decrease in genioglossus muscle activity, the base of the

Anatomy and Physiology of the Upper Airway during Sleep

The UA is a complicated structure, usually divided into four anatomical subsegments: the nasopharynx, between the nares and hard palate; the velopharynx, between the hard palate and soft palate; the oropharynx, from the soft palate to the epiglottis, and the hypopharynx, from the base of the tongue to the larynx [Figure 1]. This total structure forms a passageway for movement of air from the nose to the lungs, and also participates in many competing physiological functions such as phonation and deglutition.9 The UA is surrounded by 20 or more muscles, known collectively as UA muscles, which actively constrict and dilate the UA lumen.10 These muscles can be broadly classified into four groups: muscles regulating the position of the soft palate, tongue, hyoid apparatus, and the posterolateral pharyngeal walls. These muscle groups interact in a complex fashion to determine the patency of the airway. The mandible and hyoid bones are the main craniofacial bony structures that determine the airway’s size.11 As there is no rigid structural support, the shape and size of the UA is dependent upon the position of soft tissue structures, like the soft palate, tongue, and the walls of the oropharynx. Radiographic images show that the narrowest region in both patients with OSAS and non-obese controls, while awake, is the region posterior to the soft palate.12,13 The cross sectional area of this retropalatal region is smaller in OSAS patients than in non-obese controls.
Rajesh P Poothrikovil and Mohammed A Al Abri

Polysomnography (PSG) takes multiple physiological measurements and is an excellent tool for evaluating sleep disorders.27 Snoring can be detected and evaluated by means of small sensors in the form of piezo crystals or dynamic microphones taped laterally to the thyroid cartilage, or by utilising a nasal pressure transducer which continuously samples nasal air turbulence through a cannula. PSG provides an opportunity to assess the consequences of SDB, such as nocturnal desaturation, frequent arousals, and excessive day time sleepiness, and also plays an important role in the titration of continuous positive airway pressure (CPAP) treatment.

Figure 2: A 30-second epoch of a full night polysomnographic recording of non-rapid eye movement (NREM) sleep stage II (N2). Note the periodic snoring signals in the snore channel.

The palatopharyngeal muscle is of anatomical importance in the pharynx as it forms the internal longitudinal muscular layer around the wall of the pharynx. The muscle is located at the major site of obstruction in patients with OSAS and is therefore exposed to the vibration and stretch induced by heavy snoring and obstructive breathing.28,29 It has been reported that long term employment which involves the use of vibrating tools such as jack hammers can cause local nerve lesions in the hands.30,31 Researchers observed pathological changes in the vibration-exposed fingers, including a marked loss of nerve fibres suggestive of demyelinating neuropathy in the peripheral

tongue may push against the anterior wall of the soft palate causing narrowing of the velopharynx. Reduction in the traction between the tongue and the soft palate may increase the collapsibility of the velopharynx. Apnoeas were shown to resolve with a burst of genioglossus EMG activation. It has been demonstrated that the velopharynx is the primary site of narrowing in 80% of patients, whereas two or more sites of narrowing are commonly observed in 82% of these.24 An evaluation of the static properties of the pharyngeal wall and its surrounding muscles revealed a fundamental difference between the airway of the control subjects and those with OSAS in that the airway was closed at atmospheric pressure in subjects with OSAS, while active negative pressure was required to close the controls’ airways, even in the absence of UA muscle activity.25

One of the commonest consequences of the changes in the properties of the UA that occur during sleep is the occurrence of snoring. The snoring sound is the result of vibrations of the soft tissues of the pharynx, soft palate and uvula having specific acoustic characteristics with frequencies ranging from 5 to 136 Hz.26 SDB, such as snoring and other obstructive events, could be easily detected with a polysomnography (PSG) recording [Figure 2]. Polysomnography
Snoring-induced Upper Airway Nerve Damage

**THERMAL SENSITIVITY**
Larsson et al. reported an impairment of thermal sensitivity in the oropharynx of patients with OSAS as compared with non-snoring age-matched control subjects. Some patients with OSAS were completely unable to differentiate between heat and cold while tested on the tonsillar pillars, whereas no differences was noted at the tip of the tongue in patient and control groups, which indicates a local sensory dysfunction. They postulated that snoring-related vibrations and the deformation of UA structures in the case of apnoeas could lead to a very local pharyngeal sensory neuropathy, which could contribute to UA dysfunction during sleep. As there were only OSAS and non-snoring control groups in this study, a comparison between apnoeic snorers and non-apnoeic snorers was not possible.

**VASODILATION**
In another study, laser Doppler perfusion monitoring combined with electrical stimulation (a method used to test vascular reactivity) was performed in the mucosa of the soft palate in patients with various degrees of UA obstruction and control subjects. Habitual snorers and patients with mild OSA showed exaggerated vasodilation as compared to controls. This could be the result of minor lesions with consequent re-innervation which increased the sensitivity to mechanical stimuli. In contrast, patients with severe OSAS showed significantly reduced vasodilation as compared to controls, which could be due to the almost complete loss of afferent C-fibres, representing a permanent injury. These disturbances in the micro-circulation indicate the presence of a local afferent nerve lesion with a progressive nature in heavy snorers, both those with and without OSAS.

**SENSORY FUNCTIONS**
Kimoff et al. assessed sensory functions of the UA (oropharynx) using two-point discrimination and vibration sensory threshold methods in snorers and OSAS patients, and compared with age-matched controls. They also assessed two control points (lower lip and hand) for each subject. This study showed that the sensory detection threshold using both methods was significantly increased in snorers and OSAS patients as compared to controls. Importantly, there was no significant difference between snorers and patients with OSAS. In contrast, the sensory threshold at control sites was similar in patients and controls. Vibrometry is usually employed to assess the functional integrity of the largest afferent sensory fibres to diagnose polyneuropathy. These findings reinforce the presence of a selective impairment of UA mucosal sensory function in patients with OSAS and in those who are heavy snorers. They suggest that this impairment may be an early change in the progression of UA obstruction during sleep, possibly developing as a consequence of vibration-related oedema or neural damage during snoring. Interestingly, after 6 months of continuous CPAP usage, OSAS patients showed a significant improvement in vibration sensory thresholds thus providing strong evidence of the effectiveness of CPAP treatment. These results increase the importance of CPAP usage in the field of sleep medicine as an effective and non-comparable treatment. However, CPAP treatment fails to improve two-point discrimination, indicating a degree of permanent injury. Beginning CPAP treatment before symptoms worsen could be useful in limiting the severity of this permanent neural injury to the pharyngeal muscles.

**HISTOPATHOLOGIC FEATURES**
Woodson et al. analysed the histopathologic features of pharyngeal tissue. Transverse sections of the distal soft palate and uvula were qualitatively compared between apnoeics, severe snorers, and non-snorers using light and electron microscopy. Light microscopy of both apnoeics and non-apnoeic snorers revealed similar abnormalities such as mucous gland hypertrophy, focal atrophy of muscle fibres, and extensive oedema of the lamina propria with vascular dilation. No distinctive histopathologic findings were associated with the development of apnoea. Electron microscopy was used to reveal frequent focal degeneration of myelinated nerve fibres and axons in severe apnoeics. Similar histopathologic changes were

nerves. Similarly, snoring produces a low-frequency vibration which may also cause peripheral nerve injury and physical trauma.
noted in apnoeics and non-apnoeic snorers. This is an indication of a common aetiology related to snoring-induced vibration trauma to pharyngeal tissue rather than directly related to apnoea or desaturation.

DENERVATION
Friberg et al. described a proliferation (increased density of sensory nerve terminals with abnormal localisation and appearance) of nerve endings in a pattern suggestive of nerve injury in biopsy specimens from the oropharyngeal mucosa of some snorers. However, the study focused mostly on OSAS subjects.36 No such abnormalities were detected in non-snoring control subjects. Other muscle biopsy studies illustrated similar denervation type changes in palatopharyngeal muscles.37 The relationship between vibration and stretch-induced trauma was reinforced in a study which showed a significant increase of morphological abnormalities characteristic of neurogenic lesions (type grouping, fascicular atrophy, and grouped atrophy) in the palatopharyngeal muscle of the entire group of snoring patients as compared to non-snoring controls.38 They observed that the degree of muscle pathology increased in parallel with the proportion of obstructive breathing during sleep. This indicates that the proportion of the total sleep time spent in periodic obstructive breathing may be a surrogate quantitative measure of the magnitude of the snoring trauma to the pharyngeal tissues. Another finding in this study is that the vibration trauma of habitual snoring itself could initiate a local neurogenic lesion in vulnerable patients, before the additional trauma of stretch caused by periodic obstructive breathing. Palatopharyngeal muscle hypertrophy noted in some snorers could be neurogenic and could be due to the chronic stretching of innervated and denervated muscle fibres and/or overuse of partially denervated muscles.39

NEUROPHYSIOLOGICAL ASSESSMENTS
Finally, in a recent study, Svanborg conducted neurophysiological assessments of UA muscles by recording concentric needle EMG activity of palatopharyngeal muscles in 12 OSAS patients.40 Ten out of 12 cases showed reduced EMG activity (recruitment pattern) at maximal voluntary effort with long and polyphasic (increased duration) motor unit potentials. These features typify motor neuropathy (chronic denervation and reinnervation). Two patients showed spontaneous denervation activity (fibrillations and positive waves) suggestive of an active neuropathic process. Such findings were present in only 3 out of 15 habitual snorers. This study was of great importance in that it gives strong electrophysiological evidence of motor neuropathy in the UA muscles of OSA patients. These findings reinforce the causative role of peripheral neurogenic lesions, in the progression from habitual snoring to clinical OSAS.

Upper Airway Neuropathy in Progressive Snorers’ Disease
It is obvious that the local UA afferent (sensory) and efferent (motor) nerve lesions are present due to snoring-induced vibration trauma in some patients with snoring and in most patients with OSAS. It has been reported that the higher sound intensity in apnoeic snorers versus non-apnoeic snorers is a result of greater negative pressures on the resumption of breathing, resulting in high flow rates, turbulent flow, and greater forces on the vibrating structures.41 Several studies indicate that airway patency depends on a reflexogenic mechanism of afferent and efferent nerve pathways in the mucosa and upper airway muscles.42,43 This reflex mechanism, as a reaction to the negative intrapharyngeal pressure, is responsible for the activation of dilatory muscles. Numerous studies have described protective UA dilator reflex responses to pulses of negative airway pressure, which act to maintain airway patency during sleep.44,45 This reflex is assumed to be mediated by intra- or submucosal mechanosensory receptors. The neural drive to the UA dilator muscles is integrated at the level of brainstem motor nuclei where multiple neural inputs combine to produce a unitary output to the muscles.46 Neurogenic lesions affecting upper airway muscles impair the ability of its reflexogenic dilation, leading to increased possibility of UA collapse. A reduced pharyngeal lumen and other risk factors (i.e. obesity and anatomic abnormalities) lead to an increased degree of periodic obstructed breathing. This causes more morphological abnormalities and neurogenic lesions, which supports the hypothesis of the progressive nature of snorers’ disease.
Causes and Treatment Options for Snoring

Other causes of habitual snoring, such as nasal septal deviation, nasal valve obstruction, chronic nocturnal nasal congestion, and craniofacial abnormalities should be well identified. Patients with chronic nasal obstruction often struggle to tolerate nasal CPAP. Humidification of inhaled air, correction of potential leakage of the nasal mask, and a trial of an oro-nasal mask are initial steps that can be considered to acclimatise patients to the CPAP treatment. Patients who still cannot tolerate CPAP, or have obvious nasal polyps or a distinctive abnormality of the nasal anatomy, should consider surgical treatment. Correction of nasal obstructions has been reported to be an effective treatment of OSAS in patients who have nasal obstructions, but in those with craniofacial abnormalities, correction has proved ineffective.

Improving nasal patency by external nasal dilators has some beneficial effects on subjective snoring, but not in patients with apnoeas. Current evidence suggests that the nose may not play a significant role in the pathogenesis of OSA, but it seems to be of some relevance in the origin of snoring.

Obesity is an independent risk factor for the development of snoring. Simple snoring can be treated with general measures, including weight control and loss, avoidance of detrimental habits and toxic substances that interfere with sleep, modification of sleeping position and physical exercise. Advancement of the mandible using a dental appliance has been shown to reduce the severity of OSA. It is an effective alternate to CPAP in the treatment of snoring and milder form of OSAS. Variable mandibular advancement devices have also been successful in the treatment of patients with severe OSAS. Because the tongue attaches to the mandible directly, the tongue is expected to move anteriorly with the forward displacement of the mandible, thus improving oropharyngeal airway patency. However, no studies have been published to prove the efficacy of mandibular advancement devices in the improvement of upper airway neural injury in snoring patients.

Conclusion

In summary, the progressive nature of OSAS can be partly explained neurologically. OSAS begins with snoring-induced vibration trauma of nerves associated with the UA muscles. Histopathological, neurological, and neurophysiological signs of nerve lesions are detected in simple snorers without obstructive episodes. Periodic obstructive breathing phases expressed as a fraction of total sleep time could be a quantitative measure of the magnitude of snoring trauma to the pharyngeal tissues. Subjects with habitual snoring at risk of development of OSAS should be identified early. Beginning CPAP therapy before symptoms worsen should be considered as a preventive measure against permanent UA neuronal injury. Other options such as weight loss in obese individuals, surgical intervention for nasal obstructions, and mandibular advancement devices for craniofacial anomalies and narrow airway can also be considered in suitable patients, especially those who cannot tolerate CPAP. Studies of novel techniques may help in developing protocols to assess and manage habitual snorers.

ACKNOWLEDGEMENTS

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Emerging Burden of Frail Young and Elderly Persons in Oman

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Abstract: Recent improvements in health and an increased standard of living in Oman have led to a reduction in environment-related and infectious diseases. Now the country is experiencing an epidemiological transition characterised by a baby boom, youth bulge and increasing longevity. Common wisdom would therefore suggest that Omanis will suffer less ill health. However, a survey of literature suggests that chronic non-communicable diseases are unexpectedly becoming common. This is possibly fuelled by some socio-cultural patterns specific to Oman, as well as the shortcomings of the ‘miracle’ of health and rapid modernisation. Unfortunately, such new diseases do not spare younger people; a proportion of them will need the type of care usually reserved for the elderly. In addition, due to their pervasive and refractory nature, these chronic non-communicable diseases seem impervious to the prevailing ‘cure-oriented’ health care system. This situation therefore calls for a paradigm shift: a health care system that goes beyond a traditional cure-orientation to provide care services for the chronically ill.

Keywords: Chronic disease; Non-communicable diseases; Transition, demographic; Disability; Burden of illness; Oman.

In the majority of the countries around the world, there is a variability of human lifespan, with the Japanese having the longest living population.1 Although it is widely assumed that ageing or longevity or senescence is not a ‘disease,’ and while Erikson2 has portrayed old age as time of culmination of ‘wisdom’ that could be a gift for the succeeding generation, ageing does have its own unique challenges. Every health practitioner will attest to the view that longevity and the resultant ageing process often herald not only decreased vitality and capability, but also increased impairment, disability and a compromised quality of life.3,4 The question is whether Oman should now be concerned with the welfare of the elderly even while its population

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there is an unusual trend whereby youth people are seeking types of health care often perceived as only relevant for the elderly. Such a trend is likely to have been fostered by the following five interrelated factors.

**THE CHALLENGE OF NON-COMMUNICABLE DISEASES**

Oman has generally triumphed over communicable disease.\(^1\)^\(^2\)\(^1\)\(^1\) The country now faces the challenges of a rising tide of non-communicable diseases, sometimes labelled ‘diseases of affluence’.\(^7\) These ‘elderly-onset’, intransigent, and debilitating diseases seem to be affecting Oman’s youngsters.\(^12\)\(^-\)\(^14\) Such an emerging pattern of disease would suggest the need for a different approach in order to ensure enlightened health care planning and resource allocation. As will become apparent below, many of these emerging diseases of affluence are triggered by lifestyle changes and combatting them will require concerted efforts in the domain of rehabilitation and remedial services rather than simply curative medicine.\(^15\)

**Road traffic hazards**

Another contributor to impairment, disability and handicap in Oman is what is referred to as ‘flying coffins’, the mishap that happens to motor vehicle and their occupants on the road.\(^16\) Unsubstantiated data published in the media reveal that the road accident rate in Oman is 28 per 100,000 of the population; if true, this is likely to be highest in the world.\(^17\) It has been well established that although an ‘accident is an accident’, road traffic injuries are a major public health problem in Oman disproportionately affecting the section of the population under 40 years of age.\(^17\)\(^-\)\(^18\) The type of health care provision needed, if the claim of a tsunami of road traffic accidents is substantiated, would parallel that often provided for the elderly.

**Congenital diseases**

New reports suggest that Oman is not immune to congenital and inheritable genetic diseases as well those that are thought to be triggered by new mutations.\(^19\)\(^20\) As consanguinity is intimately embedded in Omani culture (due to the practice of first cousin marriages), this is likely to exacerbate the development of diseases that owe their origin to inherited genetic traits and health impairing
In less than three decades, a once impoverished people has experienced such dramatic health care changes that Oman was recently voted by World Health Organization as one of the most efficient health care systems in the world. This ‘miracle’ has triggered some unforeseen consequences. Despite spending only 2.4% of its of gross domestic product on health, the health care system in Oman has been equipped with versatile medical technology capable of saving lives once deemed beyond redemption. Medical conditions that previously appeared impervious to medical treatment are now treatable to the extent that patients can survive and regain some quality of life. The paradoxical consequence of this a miracle is that people whose lives are saved by medical technology will nonetheless live with severe physical, cognitive and emotional impairment, disability and handicap. Many of them will require a type of palliative care often reserved for the elderly.

Mental Illness
By definition, mental illnesses are associated with persistent and pervasive cognitive, emotional and behavioural disorders (CEBD). A sufferer is likely to have a compromised quality of life. Therefore, mental illness is one of the contributory factors to the magnitude of the problem under scrutiny here, namely the growing number of MCI. Despite this, CEBD have largely been relegated to a less prominent position in the algorithms of health care. In general, in the countries labelled ‘emerging economies’, concerted efforts to improve the welfare and care of MCI due to CEBD are ostensibly absent. Instead, health care priorities are still the perceived enemies of health such as infectious diseases and reproductive, maternal, and child health conditions. This is similar to the situation in industrialised countries that have so far focused their attention on the prevention and treatment of cancer and heart diseases. However, such a prioritisation appears to be myopic when one considers the enormous negative repercussions of CEBD. Despite their protean nature, when defined using disability-adjusted life year (DALY), CEBD appear to outstrip all other medical conditions in term of number of years lost due to ill-health, disability or early death. This is consistent with the view that CEBD tend to compromise the very essence of being human, namely, the capacity to think and act rationally. It is worth noting that CEBD tend to peak when afflicted individuals are still at a young age, thus depriving them of meaningful existence for many years. This has obvious implications for society. In addition to impairment, disability and handicap, CEBD tend affect other areas of health. For example, emotional disorders tend to have a strong link with physical illness. The relationship between emotional disorders and physical illness has been unequivocally shown in emerging literature, including in Oman.

In addition to this, there is strong evidence to suggest that some well known physical illnesses tend to create a psychological burden. For example, following diagnosis of cancer, some individuals may succumb to reactive depression which, in turn, can affect the prognosis. The Omani population, with its ‘baby boom’, ‘youth bulge’ and increased longevity, should therefore expect to see an exponential increase in the number of the people succumbing to CEBD. The available data are consonant with such a view. Although sometimes framed in the local idioms of distress, CEBD are widely recognised in Oman. The magnitude of some CEBD (e.g. deliberate self-harm, hyperkinetic disorder, depressive symptoms, factitious disorder and eating disorders in the form of deliberate food restriction) is much lower compared to international standards, but Oman is the ‘world leader’ in those distresses that owe their origin to social and cultural patterning (e.g. social
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MCI who tend to ‘over-stay’ are likely to be too frail to be discharged home—as has been found in other Arab countries.45-47

**NEW TYPES OF HEALTH CARE SERVICES**

The importance of improving neurobehavioural rehabilitation in Oman was previously highlighted;43 here, it is worthwhile discussing the relevance of the compensatory efforts needed to support MCI with persistent and debilitating medical conditions.27 Health care services should enable MCI to reach and maintain their optimal levels of physical, sensory, intellectual, psychological and social functioning in order to achieve a measure of self-determination and meaningful and independence existence.44 Due to their focus on chronic disease, modern cure-based hospitals may be the least attractive option. Rehabilitation or remedial services need multidisciplinary medical teams, with a range of skills from social work to neurosurgery, which are also supported by educational/vocational institutions and other social agencies.

If the available data circulating in the media would bear scientific scrutiny, it appears that 0.3 to 0.4% of Omanis are likely to incur impairment, disability and handicap arising from road accidents. This trend dovetails with the present discourse that Oman is likely to experience an increased number of youngsters with MCI. Extrapolating from this trend, it could be thought that some MCI are likely to use acute hospital beds as a ‘care home’. Extended hospital stays for MCI can often trigger bed shortages for other clinical populations and result in increased health care expenditure. Some of the phobias43 and dissociative disorders42).

**Possible Solutions to this Emerging Issue**

With the rising tide of non-communicable diseases; impairment, disability and handicap triggered by road traffic behaviour; some of the consequences of the modern medical revolution, and the enduring cultural patterns that may sustain genetically determined disorders, Oman needs to contemplate a new direction for its health care system. Rather than focusing on environment-related and infectious diseases, an integral part of Oman’s health system should be meeting the needs of MCI through remedial services—since it would be an untenable aspiration to find a cure for all the causes of impairment, disability and handicap in Oman.

**CARE IN THE FAMILY**

Care for MCI often depends on the prevailing Zeitgeist and history is full of approaches to helping those who are deemed unfit or dependent. Nowadays, health care facilities are mushrooming in different parts of the world to cater to the needs of MCI. These are specifically designed to provide a place of abode for MCI who cannot independently undertake their activities of daily living. In the present discussion, such health care facilities aim to provide a compensatory mechanism so that MCI can have a meaningful existence.

Thesiger fondly praised Omanis for “…their sense of fellowship, … their generosity and sense of hospitality; their dignity and their regard which they have for the dignity of others as fellow human beings.” (Cited in Smith p.541).48 It is not clear what impact modernity (as result of acculturation) has had in recent times on such an ideal humanity. Nonetheless, in family-oriented societies like Oman, interdependence is still encouraged. Such cultural patterning means that MCI will be cared for in the realm of the family. It is a widely held belief (though one that lacks empirical support) that given this type of society the fate of MCI is likely to be favourable. The question, however, is whether the modern Omani family is equipped to provide the family care needed by MCI. It has been indicated that recent affluence in Oman has resulted in the nuclear family supplanting the traditional extended family leading to a reported emergence of socially valued individualism and the erosion of interpersonal relationships that stems from modern education systems.49,50 There are also anecdotal reports indicating that the young generation “has little time for elderly people”.51

It is not clear, however, what implication this sociological observation has on the welfare of MCI. Despite such caveats, the family plays a central role in Omani society. On these grounds, it would be essential to contemplate a health care model that has affinity to Omani socio-cultural teaching.

Although, to our knowledge, there is published work, relating to the elderly, articles in the popular media indicate that the country is “not encouraging the establishment of such homes because we still
believe that the Omani community will be able to take care of their elderly population as our religion and tradition teaches us to do so.\textsuperscript{52} Given the lack of organised services in Oman for the MCI, some individual initiatives have already been seen in the community. To cope with the burden of caring for MCI, with their complex physical and emotional needs, some families employ private carers who undertake the physical aspect of caring (feeding and washing). However, employing an in-house carer is limited to those who have sufficient disposable income and may not apply to the majority of Omanis. Nevertheless, the presence of private carers spares family members from the task of constant physical caring for their MCI.

**SUPPORTED HOME AND COMMUNITY CARE**

Within the context of a family-oriented society, one approach that might be appropriate for MCI in Oman is outreach services similar to home health care, otherwise known as domiciliary care or social care. As the term implies, home health care serves the myriad needs of MCI in their homes by outreach teams that include all types of health care professionals such as nurses, occupational therapists and social workers. This type of care has some subtle benefits that outweigh other approaches. First, the services will be tailor-made for the MCI's functional limitations. Second, the MCI not need to travel outside for help which may be difficult due to their medical complications. Third, the MCI will be protected from psychological trauma—the feeling of unfamiliarity that can heighten anxiety and the feeling of being uprooted from home and having to part with possessions that are usually experienced by those put in care homes. This means MCI have their health needs met within their own community which mean they are likely to remain closer to their social network of friends, neighbours and family thus mitigating loneliness, depression and other existential dilemmas. International surveys show that over 95% of MCI would prefer to stay in their own home for as long as possible.\textsuperscript{55}

Finally, for the family and society in general, such a care model is likely to be more cost effective than hospital care. There is evidence to suggest that even if MCI tend to be marked by a high level of dependency, home care is likely to be cost-effective. Such a view is supported by studies carried out in Denmark, Ireland and Italy where home-based care is generally more cost-effective for such MCI.\textsuperscript{54}

Another alternative approach is a non-residential facility that provides activities for the MCI during the day. This would mean that MCI could spend 10–12 hours per day in a setting possibly with access to a medical facility. Under this scheme, meals, social and recreational outings, and general supervision are provided by a team of experts. There are several advantages to such a proposal. First, regular proximity to health care delivery is likely to prevent re-hospitalizations as medical assessments and medications are readily available. Second, the benefit of social stimulation will emerge. MCI who would otherwise stay at home are provided with recreational activities and other social stimulations that maybe therapeutic on their own right. There are some empirical studies suggesting that social stimulation can ward off the emergence of cognitive impairment and other debilitating emotional conditions common in MCI.\textsuperscript{55} Relevant to this, while such centres could provide remedial education and rehabilitation for MCI, in the interim, caregivers would get much needed respite to seek employment or simply to recuperate from the stress of caring for MCI with their particular problems. It is worth noting in this context that many MCI are marked by erratic behaviour and a rigidity of personality that may exhaust their caregivers.

**Conclusion**

Oman has been internationally lauded for taking vigorous action to combat disease and to improve the condition of its people. Such a health service ‘miracle’, associated with an increased standard of living, has led to the progressive demographic transformation of society. Recent socio-economic trends have reduced the occurrence of environment-related and infectious diseases. Instead, there is a rising tide of death, morbidity, handicap and disability due to genetically determined disorders and other sequelae of acculturation and modernisation including road traffic accidents and the very success of the medical revolution. This has occurred in the midst of a ‘baby boom’, a prevailing youth bulge and increased life expectancy. As result of such socio-demographic trends, the country is
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Adult Sickle Cell Disease
A Five-year Experience of Intensive Care Management in a University Hospital in Oman

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Abstract: Objectives: Sickle cell disease (SCD) is an inherited disease caused by an abnormal type of haemoglobin. It is one of the most common genetic blood disorders in the Gulf area, including Oman. It may be associated with complications requiring intensive care (ICU) admission. This study investigated the causes of ICU admission for SCD patients. Methods: This was a retrospective analysis of all adult patients ≥12 years old with SCD admitted to Sultan Qaboos University Hospital (SQUH) ICU between 1st January 2005 and 31st December 2009. Results: A total number of 49 sickle cell patients were admitted 56 times to ICU. The reasons for admission were acute chest syndrome (69.6%), painful crises (16.1%), multi-organ failure (7.1%) and others (7.2%). The mortality for SCD patients in our ICU was 16.1%. The haemoglobin (Hb) and Hb S levels at time of ICU admission were studied as predictors of mortality and neither showed statistical significance by Student's t-test. The odds ratio, with 95% confidence intervals, was used to study other six organ supportive measures as predictors of mortality. The need for inotropic support and mechanical ventilation was a good predictor of mortality. While the need for non-invasive ventilation, haemofiltration, blood transfusions and exchange transfusions were not significant predictors of mortality. Conclusion: Acute chest syndrome is the main cause of ICU admission in SCD patient. Unlike other supportive measures, the use of inotropic support and/or mechanical ventilation is an indicator of high mortality rate SCD patient.

Keywords: Anemia; Sickle cell; Acute chest syndrome; Oman.

Advances in knowledge
- This study gives a descriptive analysis for sickle cell patients admitted to an intensive care unit.
- It validates the rate and causes of sickle cell patients’ admission to intensive care unit.
- The need for inotropic support and mechanical ventilation are the main mortality predictors for sickle cell patient in an intensive care unit.

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Sickle cell disease (SCD) is an autosomal recessive disease caused by an abnormal type of haemoglobin, termed haemoglobin S (Hb S). This haemoglobin is caused by the substitution of valine for glutamic acid at the sixth amino acid position of the beta chain.\(^1\),\(^2\)

There is more than one form of sickle cell disease resulting from coinheritance of Hb S with other abnormal Hb variants. Sickle cell anaemia (Hb SS) is the commonest form in the USA. Other forms include, Hb Sβ+-thalassaemia, Hb SD, Hb SC. There are rare forms result from coinheritance of other Hb variants such as D-Punjab and O-Arab with Hb S.\(^3\) SCD is much more common in certain ethnic groups and it is considered as one of the most common genetic blood disorders in the Gulf area, including Oman.\(^2\) In Oman, the incidence of sickle cell disease and sickle cell trait in Omani neonates was 0.3% and 4.8% respectively.\(^4\) Although the SCD manifestations per se do not typically necessitate critical care management, several life-threatening complications may require intensive care unit (ICU) admission. Some patients have repeated crises, which can result in damage to different organs or systems. The most common complications associated with SCD include vaso-occlusive pain crises (VOC), acute chest syndrome, severe anaemia, infection, cerebral vascular accidents, and multiorgan failure.\(^5\),\(^6\) Because of the fact that there has been little progress in fully understanding the pathophysiology of SCD and finding a cure for it, our management is primarily focusing on treating the negative sequelae and complications of the disease.\(^6\),\(^7\) This study was a descriptive analysis of sickle cell patients who were admitted with complications to the ICU at Sultan Qaboos University Hospital, Oman, over five years and investigated the predictive factors for sickle cell mortality.

**Methods**

This study was a retrospective analysis of all adult patients ≥12 years with SCD admitted to the SQUH ICU between 1\(^{st}\) January 2005 and 31\(^{st}\) December 2009. The study was approved by both the institution’s Medical Research Committee and its Ethics Committee. SQUH is a tertiary care, teaching hospital with a 12-bed ICU and haematology ward. Data were collected from the SQUH information system (HIS) and its electronic patient records (EPR) as well as the SQUH intensive care database. Information collected included presentation, co-morbidities, organ failure, organ support, length of stay in the ICU, and final outcome. Eight factors were studied as predictors for mortality for SCD in ICU. These included Hb and Hb S levels in addition to six methods of organ support: inotropes, invasive ventilation, non-invasive positive pressure ventilation (NIPPV), haemodialysis/haemofiltration, blood transfusion and exchange transfusions. The Student’s t-test was used for continuous/ordinary variables, while odds ratios (ORs), with 95% confidence intervals (CIs) were used to assess binary variables.

**Results**

A total of 49 sickle cell patients were admitted 56 times to the ICU; 25 of those admissions (44.6%) were female patients. Two patients had three admissions while three patients had two admissions each. The range of patients’ ages was 12 and 52 years, with median of 27 years. Our ICU admits patients ≥16 years old, but our protocol allows admission of specific surgical cases and trauma down to the age of 12 years.

Acute chest syndrome was the commonest reason for admission (n = 39, 69.6%) [Table 1]. Painful crises were the principal cause of admission for 9 patients (16.1%). However, VOC was present in another 16 cases in association with other major complaints like acute chest syndrome (ACS). Multiorgan failure (MOF) was the cause of admission in 4 patients (7.1%).

Neurological complications related to SCD were found in 2 patients (3.57%). One patient...
was transferred intubated from another hospital with radiological features of cerebral ischaemia and anoxic brain injury. The other patient had a subarachnoid haemorrhage.

One patient was admitted with hepatic failure associated with hepato-renal shutdown and features of hepatic encephalopathy (1.8%). Another 12-year-old patient was admitted to our adult ICU as a surgical case after laparoscopic splenectomy and cholecystectomy with severe intra-operative haemorrhage.

Eight patients were admitted through the Emergency department (14.28%) in comparison to 46 admissions (83.9%) from the ward. Only one patient (1.78%) was referred, intubated, from another hospital directly to our ICU.

The mortality for SCD in our ICU was 16.07% (9 patients), comparable to an ICU-overall mortality of 21.1% during the same period in the same institute.

Five cases were admitted with ACS and four cases with MOF.

The length of stay in the ICU ranged from 1 to 23 days. For survivors, the mean lengths of ICU stay was 5 days, while for non-survivors it was 2.7 days. This is considered to be statistically significant ($P = 0.04$).

A total of 27 admissions for those who survived were with those with no co-morbidities (57.4%) in comparison to 4 admissions among those who died (44%). The survivors’ co-morbidities can be classified into: Behcet’s disease (1); autoimmune disease (1); hepatitis (C and/or B) virus (5); liver cirrhosis (1); osteoporosis with avascular necrosis of one or more joint (6); glucose-6-phosphate dehydrogenase (G6PD) deficiency (4); nephrotic syndrome (2); asthma (2); chronic renal failure (2), and protein C deficiency with cerebral ischaemia (1). Four admissions were pregnant patients.

It should be taken in consideration that some patients had more than one medical problem or co-morbidity at the time of admission.

Co-morbidities in non-survivors can be classified into: congenital neutropenia (1); dilated cardio-myopathy (1); systemic lupus erythematosus associated with chronic renal failure (2), and nephrotic syndrome (1).

In the ICU, the level of Hb and Hb S at the time of admission was studied as a predictor of mortality. The mean Hb for both, survivors and non-survivors were similar (8.3mg/dl and 8.6mg/dl, respectively). The range of Hb was (4.4–12.5 gm/dl) for those who survived and (6.4–11.2gm/dl) for non survivors. This result is not statistically significant ($P = 0.8$).

For those who survived, the Hb S mean for 36 cases was 63% with standard deviation (SD) 21.5 (11 not available), while for non-survivors the mean Hb S for 7 admissions was 54.5% (2 not available) with SD 25.5. This result is also not statistically significant by t-test ($P = 0.4$). High-performance liquid chromatography (HPLC) was used to study Hb S through Bio-Rad variant II (Bio-Rad Laboratories, Inc., Hercules, California, USA).

Most of the patients in this study were admitted for some time in the ward and received simple or exchange blood transfusions before coming to the ICU.

The odds ratio (OR), with 95% CIs, was used to study the six organ supportive measures as a predictive for the increase in mortality [Table 2]. These supportive measures include the use of inotropes, invasive ventilation, NIPPV, haemodialysis/haemofiltration, exchange transfusion and top-up blood transfusions.

Requirement for inotropes was a good predictive for mortality (OR 117.3). It means that mortality is much more likely in SCD patient who require cardiovascular support in the form of inotropes. Eight of the 9 patients who died required inotropes. Four of those patients had MOF and another 4 ACS. Three of 47 patients who survived required inotropic support. All the three were admitted with ACS.

Invasive mechanical ventilation (MV) was similarly a good predictive for mortality as 8 of 9 patients who died required MV while another 8 required MV among those who survived (OR 39). Regarding those who required intubation and

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**Table 1:** Causes of intensive care unit admission for sickle cell patients.

<table>
<thead>
<tr>
<th>Cause of admission</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute chest syndrome</td>
<td>39</td>
<td>69.6%</td>
</tr>
<tr>
<td>Painful crises</td>
<td>9</td>
<td>16.1%</td>
</tr>
<tr>
<td>Multi-organ failure</td>
<td>4</td>
<td>7.1%</td>
</tr>
<tr>
<td>Brain insult</td>
<td>2</td>
<td>3.6%</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>1</td>
<td>1.8%</td>
</tr>
<tr>
<td>Surgical cause</td>
<td>1</td>
<td>1.8%</td>
</tr>
</tbody>
</table>

**Causes of admission Number (N = 56) Percentage**
Sickle cell vaso-occlusion may involve both the micro- and macrovasculature. It is the most important pathophysiologic event in SCD and explains most of its clinical manifestation. The median age at death in patient with SCD is 42 years for males and 48 years for females. Acute chest syndrome (ACS) is a common cause of admission and death among patients with sickle cell disease. ACS is usually caused by infection, pulmonary infarction or fat embolism. Painful crisis is the main cause of admission in those patients (90%). To reach a diagnosis of ACS, we need a triad of fever, respiratory distress and new interstitial infiltrates on chest X-ray. 

This study represents the first data collection and analysis of sickle cell patients admitted to an ICU in Oman. In SQUH, the adult 12 bed ICU admits both medical and surgical cases including trauma patients. We admit some of those patients who require non-invasive ventilation (NIV) as well because our high dependency units (HDU) setting is not completed. We also sometimes accept paediatric trauma or post surgical patients ≥ 12 years for specific reasons. Over five years there were 56 SCD admissions which represent 3.5% of total admissions in our ICU. We referred to our patients as sickle cell disease patients depending on their high Hb S level, although genotyping studies are required for all patients to confirm the Hb SS or other sickle cell types of Hb. A retrospective study in the UK reported that Hb SS was found in 84% of their ICU admission while the other 16% was Hb SC. This might possibly refer to the severity of disease expression in patients having this type of haemoglobin. All sickle cell patients’ admissions, except one, were for medical reasons. Two patients had 3 repeated admissions while three patients had 2 admissions each. These repeated admissions were divided between ACS and painful crisis. No mortality was reported among those who had repeated admissions.

Continuous veno-venous haemodialysis (CVVHD) was used in 8 admissions; four of them died (OR 8.6). Two of those who died were admitted because of ACS as a part of generalised VOC and they developed acute renal failure. The other two were admitted with systemic lupus erythmatous and chronic renal failure. For the 4 admissions that had acute renal failure and survived, 3 had ACS and one had hepato-renal shutdown.

As haemodialysis was used for both acute and chronic renal failure, it was not considered a good indicator of severe acute illness and mortality.

### Table 2: Types of organ support needed by patients admitted to the intensive care unit.

<table>
<thead>
<tr>
<th>Organ Support</th>
<th>Survivors</th>
<th>Non-survivors</th>
<th>Odd ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inotropic support</td>
<td>3:44</td>
<td>8:1</td>
<td>117.3</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>8:39</td>
<td>8:1</td>
<td>39</td>
</tr>
<tr>
<td>Non-invasive ventilation</td>
<td>27:20</td>
<td>1:8</td>
<td>0.09</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>21:26</td>
<td>6:3</td>
<td>1.2</td>
</tr>
<tr>
<td>Exchange transfusion</td>
<td>38:9</td>
<td>7:2</td>
<td>0.8</td>
</tr>
<tr>
<td>Haemodialysis/haemofiltration</td>
<td>4:43</td>
<td>4:5</td>
<td>Not Identified</td>
</tr>
</tbody>
</table>

NIPPV was studied as a predictor for mortality (OR 0.09). This ratio illustrates that mortality was very unlikely in those patients who have SCD and do require NIPPV. NIPPV was required in 28 admissions (27 survived). The only patient who died was a case of ACS who had a sudden cardiac arrest while he was on NIPPV.

Simple blood transfusion was used to support 35 SCD admissions in ICU (62.5%). A total of 29 of them survived while 6 died. The need for blood transfusion was not considered as a very good predictor for mortality (OR 1.2). Blood exchange transfusion was used in 45 admissions (80.4%), 7 of them died. The need for exchange transfusion does not predict mortality (OR 0.8).

### Discussion

Sickle cell vaso-occlusion may involve both the micro- and macrovasculature. It is the most important pathophysiologic event in SCD and explains most of its clinical manifestation. The median age at death in patient with SCD is 42 years for males and 48 years for females. Acute chest syndrome (ACS) is a common cause of admission and death among patients with sickle cell disease. ACS is usually caused by infection, pulmonary infarction or fat embolism. Painful crisis is the main cause of admission in those patients (90%). To reach a diagnosis of ACS, we need a triad of fever, respiratory distress and new interstitial infiltrates on chest X-ray.

This study represents the first data collection and analysis of sickle cell patients admitted to an ICU in Oman. In SQUH, the adult 12 bed ICU admits both medical and surgical cases including trauma patients. We admit some of those patients who require non-invasive ventilation (NIV) as well because our high dependency units (HDU) setting is not completed. We also sometimes accept paediatric trauma or post surgical patients ≥ 12 years for specific reasons. Over five years there were 56 SCD admissions which represent 3.5% of total admissions in our ICU. We referred to our patients as sickle cell disease patients depending on their high Hb S level, although genotyping studies are required for all patients to confirm the Hb SS or other sickle cell types of Hb. A retrospective study in the UK reported that Hb SS was found in 84% of their ICU admission while the other 16% was Hb SC. This might possibly refer to the severity of disease expression in patients having this type of haemoglobin. All sickle cell patients’ admissions, except one, were for medical reasons. Two patients had 3 repeated admissions while three patients had 2 admissions each. These repeated admissions were divided between ACS and painful crisis. No mortality was reported among those who had repeated admissions.

It was sometimes difficult to choose a single reason for admission as some patients may have a complex clinical presentation with more than one complaint and more than one organ involved. This complexity may be related to the nature of SCD and the sickling process. ACS was the most common cause of admission (69.6% in our ICU) compared to...
30% in Gardner’s study. All those patients required ventilatory support whether it was invasive or non-invasive. In our study, MOF (4 patients) was the third cause of admission after painful crisis with a rate of 7.1%, compared to 17% in Gardner’s study. Gardner et al. reported a higher ICU sickle cell patient mortality compared to overall ICU mortality in the same period and same institute (16.1% versus 21.1%). Gardner et al. reported that ACS was next commonest cause with a rate of 22.2% while trauma caused death in 11.1% of cases. A review of the causes of death in adult patients (age >20 years) with sickle-cell disease in Jamaica by Thomas et al. showed that ACS was responsible for 22% of death in those patients. Other common causes of death in Jamaican sickle cell patients were renal failure 15.7%, pregnancy-related problems 7.4% and sepsis 3.7%. The length of stay in the ICU ranged from 1 to 23 days. For non-survivors, 4 of 9 patients (44%) stayed for less than 24 hours. One patient with a history of dilated cardiomyopathy was admitted from the Emergency department with MOF. The other 3 patients were admitted from the ward with VOC/ACS and suddenly deteriorated. One of them had clinical and echocardiographic features suggestive of pulmonary embolism (no spiral computed tomography [CT]). The other two had an element of sepsis in addition to ACS. This result can be referred to the nature and complexity of the disease with possibility of rapid deterioration in some cases. The other explanation may be the possibility of delay of ICU admission to give intensive supportive measures especially for patient with features of sepsis.

The majority of the cases (83.9%) had been

### Table 3: Clinical data for non-survivors among sickle cell patients admitted to intensive care unit (ICU)

<table>
<thead>
<tr>
<th>Age(years)/Gender</th>
<th>Admission Hb gm/dl</th>
<th>Admission Haemoglobin S %</th>
<th>Co-morbidities</th>
<th>Days of ICU stay</th>
<th>Cause of Admission</th>
<th>Types of Support</th>
</tr>
</thead>
<tbody>
<tr>
<td>19/M</td>
<td>8.8</td>
<td>48.4</td>
<td>Nil</td>
<td>2</td>
<td>Sepsis, MOF</td>
<td>I, V, B, E</td>
</tr>
<tr>
<td>28/F</td>
<td>8.7</td>
<td>36.2</td>
<td>Nil</td>
<td>8</td>
<td>ACS, MOF</td>
<td>I, V, B, H</td>
</tr>
<tr>
<td>19/M</td>
<td>9.6</td>
<td>NA</td>
<td>SLE, CRF, Congenital neutropenia</td>
<td>1</td>
<td>ACS/PE?</td>
<td>I, V, B, H</td>
</tr>
<tr>
<td>22/F</td>
<td>7.2</td>
<td>36.5</td>
<td>SLE, CRF</td>
<td>2</td>
<td>Sepsis, MOF</td>
<td>I, V, B, H</td>
</tr>
<tr>
<td>31/F</td>
<td>6.4</td>
<td>NA</td>
<td>SLE, nephrotic syndrome</td>
<td>1</td>
<td>ACS, sepsis</td>
<td>I, V, B, E</td>
</tr>
<tr>
<td>53/F</td>
<td>7.9</td>
<td>33.2</td>
<td>Nephrotic syndrome</td>
<td>3</td>
<td>ACS/PE?</td>
<td>I, V, B, H</td>
</tr>
<tr>
<td>19/F</td>
<td>7.7</td>
<td>91.9</td>
<td>Nil</td>
<td>3</td>
<td>ACS, sepsis</td>
<td>I, V, B, E</td>
</tr>
<tr>
<td>28/F</td>
<td>9.9</td>
<td>77.8</td>
<td>Dilated cardiomyopathy</td>
<td>1</td>
<td>ACS</td>
<td>NIV, E</td>
</tr>
<tr>
<td>30/M</td>
<td>11.2</td>
<td>89.6</td>
<td></td>
<td></td>
<td>ACS, MOF</td>
<td>I, V, E</td>
</tr>
</tbody>
</table>

Legend: M = male; F = female; MOF = multi organ failure; I = inotropes; V = mechanical ventilation; B = blood transfusion; E = exchange transfusion; ACS = acute chest syndrome; H = haemodialysis; SLE = systemic lupus erythematosus; CRF = chronic renal failure; PE = pulmonary embolism; Nil = no co-morbidities; NIV = non-invasive ventilation.
admitted to the ward for some time before being moved to our ICU. Those patients received all necessary supportive measures in the ward including blood transfusion and exchange transfusion depending on their length of stay. This may mask the role of Hb and Hb S level at the time of ICU admission as an indicator for severity of the crises or even mortality. However, simple and exchange transfusions were performed as supportive measures in 62.5% and 80.4% of ICU admissions respectively depending on baseline Hb and Hb S levels and the patient’s general condition.

The main aim of red blood cell (RBC) transfusion in SCD is to prevent and resolve vaso-occlusive events that result in ACS, stroke, and other ischaemic organ damages. This transfusion can be chronic or intermittent. The effect of RBC transfusion is improving the oxygen-carrying capacity; lowering blood viscosity; diluting the concentration of Hb S, and suppressing production of sickle RBCs due to the improvement in tissue oxygenation.14,15 The indications for intermittent RBC transfusion include: acute symptomatic anaemia; sequestration crisis; aplastic crisis; acute stroke; ACS; sepsis; acute multiorgan failure, and preparation for general anesthesia or ophthalmic surgeries.14 Simple transfusion is more convenient and easier than exchange transfusion and it is more frequently used for acute transfusion, but exchange transfusion is a good option in an acute crisis patient with a higher pretransfusion Hb level or when volume overload and hyperviscosity are of particular concern.16

One of the therapeutic aims of exchange transfusion in vaso-occlusive event like ACS is to decrease the proportion of erythrocytes containing Hb S to less than 30%, thereby improving microvascular perfusion. Two volumes of red cell exchange transfusion decrease HbS containing red blood cells to less than 20%. However, a reduction in Hb S levels may not be the only explanation for the early and dramatic clinical improvement often demonstrated in patients with ACS after exchange transfusion. This is because neutrophils and platelets, which are inflammation markers, may contribute to venous stasis in the pulmonary microcirculation.14,15 Alhashimi D et al., during their Cochrane review, found that there is no reliable evidence to support or refute the effectiveness of simple or exchange blood transfusions in treating ACS.17

Inotropic support was required in 88.9% of those who did not survive in comparison to 6.4% in survivors. It is clear that this difference is basically related to the seriousness of the clinical condition and the presence of elements of sepsis and MOF in most of non-survivors. The same facts can be applied to invasive ventilation as it was required in 88.9% in non-survivors compared with 17% for those who survived. Patients who required one or both of these organ supports have a significant higher risk of mortality. By contrast, non-invasive ventilation (NIV) does not carry that risk as it is usually used for more stable patients with ACS who require some ventilatory support.

ACS may be triggered in SCD by infection. Usually the clinical presentation is similar whether it is due to infectious or non-infectious causes. Therefore, antibiotics can be considered as one of the supportive measures for those patients. Antibiotic cover as a line of treatment for those patients was not included in detail in our study.18

Finally, there are some limitations to this retrospective study. The sample size was not large; this might be overcome in future research by including multicentre data. The other point was the difficulty in assessing the direct effect of the co-morbidities on mortality. The third point was related to our hospital ICU protocol, which led to admitting some categories of sickle cell patients who would normally be treated in an HDU rather than an ICU.

**Conclusion**

SCD is a common haematological problem in Oman. ACS was the main reason for ICU admissions in our study. The mortality for SCD was slightly less than the overall ICU mortality during the same period. The need for inotropes and invasive ventilation were considered the main predictors of mortality. On the other hand, the need for non-invasive ventilation, haemofiltration, blood transfusions and exchange transfusions were not significant predictors of mortality.

**CONFLICT OF INTEREST**
The authors declared no conflict of interest.
References


Putting Research Findings into Clinical Practice

Feasibility of integrated evidence-based care pathways in otorhinolaryngology head and neck surgery at Sultan Qaboos University Hospital, Oman

*Deepa Bhargava,’ Zainab Al-Lawatia, Rashid Al-Abri, Kamlesh Bhargava

ABSTRACT: Objectives: A perception exists that clinicians in Oman are reluctant to adopt evidence-based practice (EBP). This pilot study was undertaken to study the feasibility of using EBP pathways at the point of care in otorhinolaryngology head and neck surgery. The ultimate aim was to facilitate EBP with the probability of developing a new system for implementing research findings/translational research at the clinical point of care.

Methods: A cross-sectional prospective questionnaire pilot survey of clinicians at Sultan Qaboos University Hospital (SQUH), Oman, a tertiary care medical centre, was undertaken. Respondents included 135 physicians and surgeons with between 3 months and 25 years of clinical experience and included personnel ranging from interns to senior consultants, in areas ranging from primary care to specialist care.

Results: Of those polled, 90% (95% confidence interval CI 85–95%) either strongly agreed or agreed that evidence-based practice protocols (EBPP) could help in decision making. A total of 87.4% of participants (95% CI 81.8–93%) either strongly agreed or agreed that EBPPs can improve clinical outcomes; 91.8% of participants (95% CI 87.2–96.4%) would use and apply EBPP in day-to-day care if they were available at the point of care and embedded in the hospital information system.

Conclusions: The perception that clinicians at SQUH are reluctant to adopt EBP is incorrect. The introduction of EBP pathways is very feasible at the primary care level. Institutional support for embedding EBP in hospital information systems is needed as well as further outcome research to assess the improvement in quality of care.

Keywords: Otorhinolaryngology; Surgery, head and neck; Evidence based practice; Clinical protocol; Clinical practice guidelines; Decision making; Oman

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As the volume of medical literature has expanded, the task of putting research findings into clinical practice has become increasingly overwhelming. Practitioners of evidence-based medicine (EBM) claim that it frees clinicians from practicing medicine by rote, guesswork, and variable experience. It also ends their dependence on out-of-date authorities, and enables clinicians to work with the patient, using medical literature as a tool to solve the patient’s problems. It provides the clinicians with access to what is relevant, and gives them the ability to assess the validity and applicability of that information. In other words, it puts the clinicians in charge of information, the single most powerful resource in medicine.1

EBM integrates the best research and evidence with clinical expertise and patient values. When these three elements are integrated, clinicians and patients form a therapeutic alliance which optimises clinical outcomes and quality of life.2 Although there are a vast number of translational clinical research findings in literature, not many are being applied in day-to-day clinical care. Some barriers to practising EBM are information overload with literature of doubtful validity, lack of motivation, and lack of time. One of the methods of evidence-based practice (EBP) is implementation of the best current guidelines; however, there is also an overload of information pertaining to guidelines.

Integrated care pathways (ICP) are pre-defined plans of patient care relating to a specific diagnosis, or intervention, with the aim of making the management more structured, consistent and efficient.3 The difference between ICP and EBPP is that with EBPP the level of evidence and grade of recommendation is mentioned. A search of recent literature reveals that although ICP are recent innovations, they are being adopted by clinicians in many specialties, like primary acute, cancer, and gynaecological care. Research has shown that using ICP, with a multidisciplinary team approach to care, significantly improves risk management, reduces health care costs and the length of hospital stays, and leads to increased patient and staff satisfaction.4–7

ICP in one form or another has swept over the world largely as a grass roots movement of clinical professionals. The movement has been motivated by a search for a more efficient, economical, high-quality tool that will improve the variations in patient care and outcomes.8 EBM is important in all areas of medicine, including otorhinolaryngology, and head and neck surgery (ORL-HNS).

The aims of the present study were to test the feasibility of introducing EBP and ICP into the ORL-HNS unit in the Department of Surgery at Sultan Qaboos University Hospital (SQUH), Oman; to gather facts from key personnel regarding changes and improvements they would like to see; to identify if we are being overly optimistic with regards to EBPP, and to determine the probability of developing a new system for improved quality of care.

Advances in Knowledge
- The study demonstrates the willingness of clinicians in Oman to adopt evidence-based practice (EBP) and evidence-based practice protocols (EBPP).
- The study demonstrates the feasibility of introducing EBPP and integrated care pathways (ICP) at the point of care.
- This study has the potential to lead to the innovative development of a new system for implementing research findings/translational research in the clinical setting at the point of care.
- Embedding EBPP and ICP in hospital information systems has the potential to help clinicians make decisions and apply translational research findings to clinical care, thereby raising the quality of care.
- During the process of preparing the EBPP research, gaps in knowledge were identified. These could be the targets for future research.

Applications to Patient Care
- In the future, EBP will have far-reaching implications for patient care as embedding EBPP in the hospital information system will facilitate decision making and standardise patient care.
- Since most clinicians polled believed EBPP can help in decision making and improve clinical care and outcomes, this study has demonstrated the potential for raising the standard of patient care.
- In the future, EBPP will facilitate the task of applying the latest, most accurate evidence to patient care.
- EBPP could potentially reduce wasteful spending by preventing unnecessary, outdated investigations and treatments.
Methods

A questionnaire pilot survey was conducted to determine the attitude of clinicians to EBP, the relation of EBP to improved quality of care, and the prospects of introducing evidence-based practice protocols (EBPP) in Oman. The main study on measuring outcomes of EBPP was submitted for approval to the Medical Ethics & Research Committee at SQUH. The subjects belonged to the following clinical specialties and departments: ORL-HNS, general surgery, accident and emergency, and family and community medicine. The questionnaire was clearly designed with a concise one-page layout and clear focus, and was subjected to internal and external validity tests. Internal validity was assessed by piloting the questionnaire with four experts who analysed it for validity of language, face, and content. Following this, the questionnaire was edited and arranged in a logical, brief, unambiguous and user-friendly format. Unnecessary and repetitive questions were detected and deleted. The external validity was carried out to determine whether the questionnaire measured what it was supposed to measure. Its reliability was found to be satisfactory. Random selections of doctors were invited to participate and the questionnaire was completed face-to-face. The aims of the study were clearly explained with a researcher on hand to answer questions and collect the completed questionnaire.

The questionnaire included the following nine categories/queries: 1) number of years of clinical experience and 2) practice setting. Questions 3 to 9 assessed different levels of agreement/disagreement regarding: 3) EBPP facilitating workflow; 4) the need of clinical protocols to be prepared based on best current evidence; 5) whether EBPP are preferable to routine protocols as they have a higher level of evidence and a higher grade of recommendation; 6) the respondent’s level of belief that EBPP could help in decision making; 7) the need of pathways to be problem specific since they change according to triage assessments; 8) the respondent’s feeling as to whether EBPP might improve clinical outcomes; and 9) the likelihood that the respondent would use EBPP, especially if embedded in the hospital information system. Statistical analysis was done using the Statistical Package for the Social Sciences (SPSS, Version 16, IBM, Chicago, Illinois, USA) and through a chi-square test. Various correlations were studied (e.g. between EBPP from different points of view and number of years of clinical experience). The confidence intervals (CIs) were calculated using the CI calculator for proportions.

Results

The researchers distributed 150 questionnaires and 135 completed questionnaires were returned. The range of clinical experience of respondents ranged from 3 months to 25 years [Figure 1]. Overall, 71% of participants (95% confidence intervals [CI] 63.4–78.7%) agreed that EBPP are preferable to routine protocols as EBPP are prepared based on the best current research and include level of evidence and grade of recommendation. A total of 77% of respondents (95% CI 70–80%) agreed protocols change according to triage assessments, so they need to be problem-specific.

Overall, 90% (95% CI 85–95%) either strongly agreed or agreed that EBPP could help in decision making; however, 10% disagreed that EBPP could help in decision making. Of those polled, 43% (95% CI 34.7–51.4%) strongly agreed and 44.4% (95% CI 36–52.8%) agreed that EBP protocols can improve clinical outcomes, while in total of 87.4% of respondents (95% CI 81.8–93%) expected an improvement in clinical outcomes by using EBPP [Figure 2].

Overall, a total of 91.8 % (95% CI 87.2–96.4%) of the participants, (with 53.3% [95% CI 44.9–61.7%] having strongly agreed, and 38.5% [95% CI 30.3–46.7%] having agreed) would use EBPP and apply it in their day-to-day care if it were available at the point of care through the hospital information system [Figure 3]. Figures 2 and 3 also demonstrate the correlation between the number of years of experience with the expectation of clinical
outcomes and a willingness to apply EBPP.

Discussion

The present study tested the feasibility of introducing EBP and ICP into the ORL-HNS unit in the department of Surgery at SQUH, Oman. A literature search revealed no similar survey on the feasibility of embedding EBM in care pathways; however, there have been a number of surveys of the behaviour of doctors, nurses and related professionals in regards to EBM. It was estimated in the 1970s in the USA that only around 10−20% of all health technologies then available (e.g. drugs, procedures, operations, etc.) were evidence-based; that figure improved to 21% in 1990, according to official US statistics.9

When the EBM movement was still in its infancy, Dave Sackett emphasised that evidence-based practice was no threat to old-fashioned clinical experience or judgment.1 This perception is one of the barriers to the extension of EBM practice. Greenhalgh wrote, "We clinicians would not be human if we ignored our personal clinical experiences, but we would be better off basing our decisions on the collective experience of thousands of clinicians treating millions of patients, rather than on what we as individuals have seen and felt."10 However, in spite of high levels of clinical evidence, extensive grades of recommendations, and translational research, there is still a lack of evidence-based decisions being applied to patient care at the point of care.

A pilot study for developing a model for implementing EBPP is being developed in the ORL-HNS unit in the department of surgery at SQUH. This model has multiple steps, starting from assessing the needs of EBPP, preparing the pathways, getting consensus from participating departments, implementing the pathways, and studying the outcomes by auditing the improvement in quality. One of the perceived barriers is the attitude of clinicians towards EBP; this has never been studied in Oman.

This feasibility study is important to determine the level of acceptance of EBPP prior to its implementation.

The significance of the present study was that it aimed to identify barriers to EBP and is one step towards applying the above described model and implementing EBPP.

The objectives of study have been met, as mentioned in the results, as 90% of participants strongly agreed or agreed that EBPP could help in decision making, and 87.4% of participants either strongly agreed or agreed that EBPP can improve clinical outcomes.

The ultimate aim of this study is the introduction of EBPP and ICP in ORL-HNS at the point of care by embedding the protocols into the hospital's electronic patient records system. Of special significance in the survey is the finding that 92% of the participants would use these protocols and apply them in their day-to-day care if available at point of care. A weakness of the study was that there was no control so it was difficult to assess if answers were correct or not.

There are many advantages of using a strategy of implementing EBP and EBPP. In terms of medical education for health care professionals,
self-directed, life-long learning can be achieved by EBP. Information management in the current age is a challenge, but EBP clinicians are taught to be efficient information managers. Introducing EBPP would enhance a collaborative learning strategy between the otolaryngologist and the primary care clinician. EBPP can also help improve the quality of care by solving clinical dilemmas at point of care, especially in the primary care setting. The users of EBPP, especially junior doctors, will be supported by the best evidence upon which to base their decisions rather than blindly following their seniors. There is the potential for EBPP to reduce wasteful expenditure that can occur when unnecessary or outdated investigations and treatments are ordered. In dealing with clinical problems, health professionals often differ in their approaches and opinions. There is a need for team work and a multidisciplinary approach to patient care which is facilitated by following EBPP. Quality requires the maximisation of benefits and minimisation of risks for the patients. For these reasons, 90% of participants believe EBPP would improve the quality of care. Finally, EBPP can lead to new research areas as, during the process of preparing the EBPP, research gaps could be identified and direct future research.

However there are also disadvantages of EBPP. There can be a limited applicability of evidence. This is possible, especially in patients with comorbid conditions. The clinical expertise of the clinician should be relied on in these situations; however, working with the best knowledge available is usually better than having no idea at all. Further disadvantages can be a lack of high-grade evidence, controversial evidence, inconsistent evidence, or incoherent evidence. In spite of this, based on unpublished research, we have found fairly good levels of evidence for common ORL-HNS conditions. A final disadvantage of EBPP would be the potential for limiting the learning for junior doctors. One of the participants, who was against EBPP, even mentioned that it is like “spoon-feeding residents”. We disagree with this statement. Since most of the self-directed learning for residents is in order to pass examinations, they rarely find the time to ask the clinical questions which are vital to EBP. Moreover, critical appraisal and EBM language is routinely taught in journal clubs.

Based on this questionnaire survey, our recommendations are: 1) EBPP are preferable to routine protocols as they provide a rigorous and acceptable framework for making complex decisions at the point of care; 2) embedding EBPP in hospital information systems would enhance EBP at the point of care and improve the quality of patient care for ORL-HNS conditions at the primary care level; 3) EBM requires institutional support by way of specialist skills, a supply of evidence, and embedding EBPP in hospital information systems, and 4) further outcome-based research is needed to study the degree of quality improvement after implementing the described EBPP.

**Conclusion**

The perception that ORL-HNS doctors in Oman are reluctant to adopt changes in EBP is incorrect.
Most clinicians, including otolaryngologists, believe EBPP can help in decision making and improve clinical outcomes.

The feasibility of introducing otolaryngology EBPP for use at the primary care level is very high. Embedding EBPP in hospital information systems would enhance EBP at point of care and help provide the benefit of research findings in the clinical care setting.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

References

عملية استئصال ورم الرحم العضلي أثناء إجراء العملية القيصرية: إمكانية إجراء العملية والسلامة

لوفينا ماتشادو، فيدياناثان غوري، نهال الريامي، لاميا الخروصي

الهدف: مراجعة حالات الاستئصال القيصرية أثناء إجراء العملية القيصرية، وتحديد الإجراءات الطارئة المستخدمة في هذه الحالة.

التوافر: تم استخدام نظام إدارة المخاوف في جامعة سلطان قابوس في عمان، وتم استخراج 8 حالات من أقدم 15 حالة تم ملاحظتها.

النتائج: في كل حالة، تم استخدام إجراءات طارئة لتحكم الإفراط في نزيف الدم، وتم استخدام أدوية مضادة للكميات المثيرة للفوlements.

اللقاء: استئصال الورم أثناء إجراء العملية القيصرية، وتحديداً في الحالات التي لا يوجد فيها ناقل مبيض، يمكن أن يكون مفيدة.

مفتاح الكلمات: استئصال الورم، إجراء العملية القيصرية، نزيف، يتوقف، نفاذ، أمزاج.
The incidence of myoma associated with pregnancy is reported at 0.3–5%, with a majority of myomas not requiring surgical intervention during pregnancy or delivery.¹–⁴ Myomectomy at the time of a Caesarean section has traditionally been discouraged due to fears of intractable haemorrhage and increased postoperative morbidity. However, a number of authors have recently shown that myomectomy at Caesarean does not increase the risk of haemorrhage.²,¹⁰–²¹

We present a series of 8 cases where myomectomy was performed during Caesarean section for large lower segment fibroids ranging in size from 4 to 12 cms. The antenatal course, perioperative management, and postoperative morbidity are discussed.

Methods

We performed a retrospective cohort study of 8 patients with myomas which resulted in pregnancy complications. All 8 patients underwent myomectomy at the time of Caesarean section at Sultan Qaboos University Hospital (SQUH) between January 1999 and December 2010. Ethical approval for the study was obtained from the University Medical Research and Ethics Committee (MREC #399). Patients’ medical records were perused for demographic data, parity, and antenatal course, type of Caesarean section, size and location of the fibroids, blood loss, postoperative morbidity, and neonatal outcome. All of the women in the study fulfilled the following five criteria: 1) documented fibroid during the index pregnancy by antenatal ultrasound or at surgery; 2) delivery by Caesarean; 3) no evidence of antenatal bleeding; 4) no other procedure at Caesarean apart from myomectomy, and 5) no pre-existing coagulopathy. Informed consent was obtained from all patients preoperatively. Of the 8 patients studied, 7 had anterior lower segment fibroids and one had a posterior lower uterine fibroid which interfered with closure of the uterine incision. Adequate blood and blood products were arranged preoperatively.

Myomectomy was performed in the conventional fashion using an incision over the myoma, enucleating it, and obliterating the dead space in two to three layers using interrupted 1-0 Vicryl sutures (Ethicon Inc., New Jersey, USA). Anterior lower segment myomas encroaching on the proposed incision line were excised prior to delivery of the baby while the others were removed after the baby had been delivered. The Caesarean incision was closed in 2 layers with 1-0 Vicryl sutures. High dose oxytocin was used intraoperatively and postoperatively, and some patients required additional uterotonic agents. Blood loss was estimated from suction aspiration, and from weighing mops, swabs and drapes used during surgery. Prophylactic antibiotics were administered to all the patients. A review of literature was performed using PubMed, Medline, and Google.

Results

The average age of the women was 28.7 years. The age, parity, and associated risk factors of the patients; factors, size and location of the myomas; the operative findings and incisions used during surgery, and the complications and neonatal outcomes are summarised in Table 1. Of those in the study, 7 of the 8 patients had lower segment anterior wall fibroids at or close to the incision site, and one patient had a large posterior wall fibroid which projected through the uterine incision after delivery of the baby and needed removal to facilitate...
Caesarean Myomectomy
Feasibility and safety

In total, 4 were intramural fibroids (50%) and 4 were subserous. The size varied from 4–12 cm with 7 of them being larger than 5 cm in diameter. Regarding intra-operative blood loss, 1 patient lost 900 ml, 5 patients lost 1–1.5 litres, 2 lost 1.5–2 L, and 1 patient with a 10 x 12 cm subserous fibroid lost 3.2 L. Stepwise devascularisation was needed to control atonic postpartum haemorrhage (PPH) in 1 patient. Preoperative placement of uterine balloon catheters was used in another patient with a large posterior wall fibroid. The balloon was inflated intra-operatively after delivery of the baby, effectively controlling the haemorrhage. None of the patients required hysterectomy.

Neonatal outcome was good in all the patients. The mean gestational age at delivery was 36.75 weeks (range 33–38 weeks). The 5 minute Apgar score was 9–10 in all the newborns with birth weights ranging from 2160 grams (preterm 33 weeks) to 3,000 grams.

Table 1: Demographic and clinical profile, operative findings and outcome of the patients who underwent Caesarean myomectomy at our institution

<table>
<thead>
<tr>
<th>Age/Parity G/P/A</th>
<th>Risk factors/ co-morbidities</th>
<th>No. &amp; location of fibroids</th>
<th>Size at start of pregnancy</th>
<th>Size at CS</th>
<th>GA at CS in wks</th>
<th>Est. blood loss in ml</th>
<th>Baby details</th>
<th>Incision</th>
<th>Postoperative morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 yrs G6/P1/A4</td>
<td>Prev 1 CS Inframural LUS anterior wall + multiple small fibroids</td>
<td>Intramural fibroids</td>
<td>6.2 x 4.3 cms</td>
<td>7 x 6 cms</td>
<td>38</td>
<td>1,100</td>
<td>Female</td>
<td>Pfannenstiel UT-Lower seg transverse</td>
<td>None</td>
</tr>
<tr>
<td>19 yrs G1</td>
<td>Essential HT PPROM 32 w Betamethasone x 2 doses Lower segment left side. Subserous</td>
<td>8.6 x9.1 cms</td>
<td>9 x 9 cms</td>
<td>Infarction</td>
<td>33</td>
<td>1,100</td>
<td>Female</td>
<td>Vertical SUMLI UT-Low vertical ROP deflexed head</td>
<td>None</td>
</tr>
<tr>
<td>35 yrs G4/P3</td>
<td>None Lower segment ant. Wall Intramural</td>
<td></td>
<td>9x10 cms</td>
<td>8 x 8 cms</td>
<td>38</td>
<td>1,500</td>
<td>Male</td>
<td>Pfannenstiel UT-Lower seg transverse</td>
<td>Blood transfusion</td>
</tr>
<tr>
<td>24 yrs G2/P1</td>
<td>Breech, polyhydramnios. Prev. multiple myomectomy (4). Cavity not entered Lower segment anterior wall Intramural</td>
<td></td>
<td>6 x 7 cms</td>
<td>8 x 7 cms</td>
<td>38</td>
<td>1,100</td>
<td>Female</td>
<td>Pfannenstiel UT-Lower segment transverse</td>
<td>None</td>
</tr>
<tr>
<td>28 yrs G2/P1</td>
<td>Previous LSCS PIH Lower segment posterior wall Subserous</td>
<td></td>
<td>6.5 x 5.5 cms</td>
<td>6.5 x 6 cms</td>
<td>38</td>
<td>1,100</td>
<td>Female</td>
<td>Pfannenstiel UT-Lower segment transverse</td>
<td>Blood transfusion</td>
</tr>
<tr>
<td>38 yrs G5/P4</td>
<td>None Lower segment rt side anterior Subserous</td>
<td></td>
<td>9.8 x 7 cms</td>
<td>10 x 12 cms Degen.</td>
<td>37</td>
<td>3,200</td>
<td>Male</td>
<td>Vertical SUMLI UT-High lower segment transverse</td>
<td>Anaemia</td>
</tr>
<tr>
<td>28 yrs G1</td>
<td>PIH Lower segment anterior Subserous</td>
<td></td>
<td>6 x 5 cms</td>
<td>7 x 5 cms Haem.</td>
<td>37</td>
<td>900</td>
<td>Female</td>
<td>Pfannenstiel UT-Lower segment transverse</td>
<td>None</td>
</tr>
<tr>
<td>32 yrs G9/P2/A6</td>
<td>Previous 2 LSCS Upper part of lower segment anterior Intramural</td>
<td></td>
<td>4 x 4 cms</td>
<td>4 x 4 cms Calcified</td>
<td>35</td>
<td>2,000</td>
<td>Female</td>
<td>Pfannenstiel UT-Lower segment transverse</td>
<td>Blood transfusion</td>
</tr>
</tbody>
</table>

Legend: G/P/A = gravida/para/abortion; CS = Caesarean section; GA = gestational age; LUS = lower uterine segment; HT = hypertension; PPROM = preterm premature rupture of membranes; SUMLI = subumbilical midline longitudinal incision; ROP = right occipito-posterior position; UT = uterus; LSCS = lower segment Caesarean section; PIH = pregnancy induced hypertension; PPH = postpartum haemorrhage; PRBC = packed red blood cells, FFP = fresh frozen plasma; Apg = Apgar score at 1 and 5 minutes.
Discussion

Uterine myomas are found in approximately 0.3–5% of pregnant women, with the increasing incidence attributable to the fact that more and more women are delaying childbearing.1–4 One in ten of these women will have complications during pregnancy that are related to the myoma. A great majority of myomas associated with pregnancy remain asymptomatic and do not require treatment, with about 22–32% showing increased growth.5 Larger fibroids (>5cm) are more likely to grow during pregnancy and can cause miscarriages, obstructed labour, malpresentations, pressure symptoms, pain due to red degeneration, preterm labour, preterm premature rupture of membranes,

Table 2: A comparison of various studies on Cesarean myomectomy

<table>
<thead>
<tr>
<th>Authors</th>
<th>Roman11</th>
<th>Kwon14</th>
<th>Kaymak11</th>
<th>Ehigiegb13</th>
<th>Ortac10</th>
<th>Ahikari17</th>
<th>Omar19</th>
<th>Machado LSM</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. and type of cases</td>
<td>368</td>
<td>88</td>
<td>120</td>
<td>25</td>
<td>22</td>
<td>14</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Maternal Age</td>
<td>11 CM</td>
<td>257 CS</td>
<td>NA</td>
<td>40 CM</td>
<td>80 CS</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Parity</td>
<td>37</td>
<td>35</td>
<td>32.5±4.4</td>
<td>31.9±4.5</td>
<td>30.8±3.1</td>
<td>30.8±3.8</td>
<td>25–35 yrs</td>
<td>28.75</td>
</tr>
<tr>
<td>Para 0</td>
<td>NA</td>
<td>NA</td>
<td>84.1%</td>
<td>0.8±1.2</td>
<td>1.1±1.1</td>
<td>13</td>
<td>NA</td>
<td>11</td>
</tr>
<tr>
<td>Para 1-4</td>
<td>NA</td>
<td>NA</td>
<td>16.9%</td>
<td>NA</td>
<td>NA</td>
<td>12</td>
<td>NA</td>
<td>3</td>
</tr>
<tr>
<td>Mean GA at CS</td>
<td>38 (27.3–41.6)</td>
<td>39 (24–42.6)</td>
<td>38±1.19</td>
<td>37.7±2.5</td>
<td>37.6±1.4</td>
<td>36.9 (29–42)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>No. of Fibroids</td>
<td>Single</td>
<td>91</td>
<td>67%</td>
<td>75%</td>
<td>10</td>
<td>NA</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Multiple</td>
<td>20</td>
<td>33%</td>
<td>25%</td>
<td>15</td>
<td>NA</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Location</td>
<td>Lower US</td>
<td>NA</td>
<td>50%</td>
<td>11 (27.5%)</td>
<td>NA</td>
<td>NA</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Upper US</td>
<td>NA</td>
<td>50%</td>
<td>22 (55%)</td>
<td>NA</td>
<td>NA</td>
<td>5</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Both</td>
<td>NA</td>
<td>-</td>
<td>7 (17.5%)</td>
<td>NA</td>
<td>NA</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pedunculated</td>
<td>NA</td>
<td>-</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Size</td>
<td>&lt;5 cms</td>
<td>Mean 3.5 (0.9–30)</td>
<td>Mean 3 (1–20)</td>
<td>NA</td>
<td>≤3cm, 2 (5%)</td>
<td>Most 2–4 cms</td>
<td>Mean 22 (9.5±4.6)</td>
<td>range 5–19 cm</td>
</tr>
<tr>
<td>5–10 cms</td>
<td>NA</td>
<td>-</td>
<td>4–5cm, 14 (35%)</td>
<td>2</td>
<td>-</td>
<td>5–19 cm</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>&gt;10 cms</td>
<td>26cm, 24 (60%)</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Operating time</td>
<td>LSCS</td>
<td>-</td>
<td>51 (20–07)</td>
<td>NA</td>
<td>-</td>
<td>44.4±6.7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CM</td>
<td>55 (25–161)</td>
<td>-</td>
<td>53.3±18.6</td>
<td>-</td>
<td>NA</td>
<td>41.6±8</td>
<td>Range 25–60</td>
<td>54.1±8.84</td>
</tr>
<tr>
<td>Blood loss</td>
<td>Blood loss</td>
<td>12.6%</td>
<td>12.8%</td>
<td>731.5 ml</td>
<td>12.5%</td>
<td>11.3%</td>
<td>876 ±312 ml</td>
<td>324.2 ml</td>
</tr>
<tr>
<td>Range</td>
<td>Significant haem.</td>
<td>400–2500ml</td>
<td>-</td>
<td>400–1700ml</td>
<td>-</td>
<td>359–600ml</td>
<td>900–3200ml</td>
<td></td>
</tr>
<tr>
<td>Postoperative Morbidity</td>
<td>Blood transfusion</td>
<td>0.9%</td>
<td>1.2%</td>
<td>1 relap. for bleeding</td>
<td>4 (10%)</td>
<td>5 (6.3%)</td>
<td>5</td>
<td>NA</td>
</tr>
<tr>
<td>Fever</td>
<td>4.5%</td>
<td>4.7%</td>
<td>12 (13.6%)</td>
<td>3 (7.5%)</td>
<td>8 (10%)</td>
<td>2 (8%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Anaemia</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>60%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>Post op Hospital stay in days (range)</td>
<td>3.6 (2–7)</td>
<td>3.4 (2–12)</td>
<td>NA</td>
<td>3.3±0.8</td>
<td>2.7±0.6</td>
<td>7.4±2.2 (3–12)</td>
<td>3.7±0.9 (2–6)</td>
</tr>
</tbody>
</table>

Legend: GA = gestational age; US = uterine segment; CM = Cesarean myomectomy; CS = Cesarean section; LSCS = lower segment Cesarean section; NA = not available or not specified; relap = relaparotomy
Caesarean Myomectomy
Feasibility and Safety

Katz et al. found that 10–30% of women with myomas associated with pregnancy had complications as listed above. Caesarean section rates in women with myomas are higher, up to 73%, mainly due to obstructed labour and malpresentations.

Preservation of the uterus without loss of its function and compromising the mother’s ability to bear more children is definitely a greater surgical achievement than a hysterectomy; hence, Caesarean myomectomy must be considered by experienced obstetricians wherever feasible. The orthodox view of one of the pioneers of myomectomy in non-pregnant women, Bonney, is reflected in his writings: “It is tempting for the adventurous and sympathetic surgeon to condense the operation of lower segment Caesarean section and myomectomy into one undertaking and save his patient the ordeal of a second admission to hospital. This kindly but misguided policy we heartily deprecate.” However, his pupils, Hawkins and Stallworthy, did advocate Caesarean myomectomy in selected cases, as in the incidence of anterior lower segment myomas on the proposed incision line.

Exacoustos and Rosetti reported that in their series of 9 cases of Caesarean myomectomy, three were complicated by severe haemorrhage necessitating hysterectomy; hence, they recommended caution while making the decision to perform this procedure. Some authors report a higher incidence of postpartum haemorrhage and puerperal sepsis if the fibroid is not removed at Caesarean section. In addition, the uterus in the immediate postpartum phase is better adapted physiologically to control haemorrhage than at any other stage in a woman’s life; hence, it seems logical to perform Caesarean myomectomy.

The management of fibroids encountered at Caesarean section remains a therapeutic dilemma. Myomectomy during Caesarean section has traditionally been discouraged due to the risk of uncontrollable haemorrhage, unless the myoma is pedunculated. Recent studies have described techniques to minimise blood loss at Caesarean myomectomy including uterine tourniquet, bilateral uterine artery ligation, and electrocautery. In our series, stepwise devascularisation was required to control atonic PPH in one patient; in another patient uterine artery balloon catheters were placed preoperatively. Several authors have now shown that in selected patients and in experienced hands, myomectomy at the time of caesarean section is a safe and effective procedure.

The experience of different authors who have performed Caesarean myomectomies is presented in Table 2, including the present series. Roman et al. compared the outcomes of 111 patients who had had myomectomy at Caesarean with 257 patients who had undergone Caesarean alone. No significant difference was found in the incidence of intra- or postoperative complications between the 2 groups; however, accurate conclusions cannot be drawn from that study as only 22.7% of the patients had fibroids greater than 6 cm in diameter (median 3.5 cm).

Kaymak et al. compared 40 patients who underwent myomectomy at Caesarean section with 80 patients with myomas who underwent Caesarean section alone. The mean size of the fibroids removed was 8.1 cms compared to 5.7 cms in the controls. The authors found no significant difference in the incidence of haemorrhage (12.5% in the Caesarean myomectomy group versus 11.3% in the controls), postoperative fever, or frequency of blood transfusions between the 2 groups, and concluded that myomectomy during Caesarean section is not always a hazardous procedure and can be performed by experienced obstetricians without any complications.

Ortac et al. reported 22 myomectomies during Caesarean for large fibroids (>5 cm) and advocate it to minimise postoperative sepsis. In another study by Burton et al., of the reported 13 cases of myomectomy at Caesarean section, only 1 case had intra-operative haemorrhage and they concluded it to be safe in selected patients.

A large retrospective case-control study by Li Hui et al. assessed the effectiveness, safety, complications, and outcomes of myomectomy during Caesarean section in Chinese women with fibroids antedating pregnancy. The study group of 1,242 pregnant women with fibroids who underwent myomectomy during Caesarean section was compared with 3 control groups: 200 pregnant women without fibroids (Group A), 145 pregnant women with fibroids who underwent Caesarean section alone (Group B), and 51 pregnant women who underwent Caesarean hysterectomy (Group C). No significant differences were noted between
the groups in the mean haemoglobin change, the frequency of haemorrhage, postoperative fever, or the length of hospital stay. These findings corroborate the fact that myomectomy during Caesarean section is a safe, effective procedure not associated with significant complications.

Further strengthening the increasing trend towards Caesarean myomectomy is yet another case series by Hassiakos et al. They compared 47 pregnant women with fibroids who underwent Caesarean myomectomy with 94 pregnant women with fibroids who had Caesarean section alone. Myomectomy added a mean operating time of 15 minutes to the Caesarean section. No patient had a hysterectomy, postpartum complications, or blood transfusion. The length of hospital stay was comparable in both groups; hence, these authors also generally recommended performing the procedure. Yuddandi reported removal of a 33.3 × 28.8 × 15.6 cm fibroid at Caesarean with an intraoperative blood loss of 1,860 ml, necessitating blood transfusion. Leanza et al. and Igwegbe et al. have also reported large myomas removed at Caesarean section.

In our series of 8 patients, 5 lost less than 1.5 L of blood and there was no significant postoperative morbidity. The patient with a blood loss of 3,200 ml had the largest myoma in this series (10 x 12 cm) which showed evidence of degeneration and also had atonicity of the uterus necessitating a higher dose of oxytocin, carboprost, and a blood transfusion. Since the fibroid was on the right anterior lower segment, a low vertical incision was used. The large size of the fibroid and atonic uterus led to the increased haemorrhage. There were no postoperative complications.

Despite the majority of the patients having large myomas and 50% being intramurally located, no hysterectomy was required in any patient. Stepwise devascularisation was necessary in one case. The size of the fibroids was confirmed by the pathology reports, and changes like haemorrhage, infarction, calcification, and hyaline degeneration were seen in 4 fibroids. Myomectomy added 15 minutes to the operating time and 1 day to the hospital stay but there was no significant postoperative complication. None of the patients had postoperative sepsis.

The limitations of this study are the small sample size and the retrospective nature of the study.

**Conclusion**

In conclusion, patient selection is crucial in Caesarean myomectomy. Large fundal intramural fibroids should be intuitively avoided. Intramural myomectomy should be performed with caution. Fibroids obstructing the lower uterine segment or accessible subserosal or pedunculated fibroids in symptomatic patients can be safely removed by experienced surgeons. The message is that what was once considered taboo should now be reconsidered.

Measures to minimise blood loss, like preoperative placement of uterine artery, balloon catheters, uterotonics drugs, uterine artery ligation, uterine tourniquets, stepwise devascularisation, and post-Caesarean uterine artery embolisation would optimise outcomes and significantly decrease the chance of hysterectomy. The time is right to recommend Caesarean myomectomy in selected patients in well-equipped tertiary settings, which could also have a positive bearing on future reproductive outcomes.

**CONFLICT OF INTEREST**

No funding was received for this study and the authors declared no conflict of interest.

**References**


Objectives: This study aimed to investigate the presence of oxidative stress and inflammation in ischaemic stroke patients by measuring malondialdehyde (MDA), total antioxidant status (TAS), and high-sensitivity C-reactive protein (hsCRP) in the early post-ischaemic period, and to determine the role of Ginkgo biloba therapy in correcting the markers of oxidative stress and inflammation. Methods: This study was conducted at Ibn Seena Hospital, Mosul City, Iraq and included 31 cerebrovascular accident (CVA) patients and 30 healthy controls. Ischaemic stroke patients were divided into two groups: group I (n = 15) received conventional therapy; group II (n = 16) received conventional therapy with G. biloba (1500 mg/day) for 30 days. Blood samples were obtained from patients and controls before treatment and assays done for serum levels of MDA, TAS, and hsCRP. For CVA patients, a post-treatment blood sample was taken and the same parameters reassessed. Results: Compared with the controls, patients’ serum levels of MDA, and hsCRP were significantly higher (P ≤0.001) and TAS significantly lower. Group I and II patients reported a significant reduction in serum levels of MDA and hsCRP and a significant increase in serum levels of TAS, in comparison with pre-treatment levels. There was no significant difference (P = 0.19) in serum MDA levels between groups I and II, whereas, serum TAS levels were significantly higher (P ≤0.001) and hsCRP significantly lower (P ≤0.01) in group II. Conclusion: Acute stroke is associated with oxidative stress and inflammatory response in the early period. G. biloba plays a potential role in reducing oxidative damage and inflammatory response due to its antioxidant, anti-inflammatory, and protective effects.
Stroke, or cerebrovascular accident (CVA), is the third leading cause of death after cardiovascular diseases and cancer. In fact, it is the second-leading cause of mortality and disease among adults over 60 years of age worldwide. Approximately 80% of strokes are ischaemic in origin, since they result either from thrombus in situ or an embolism of distant origin.

Cerebral ischaemia initiates a cascade of cellular and molecular events that lead to brain damage, with one such event being post-ischaemic inflammation. Focal cerebral ischaemia is associated with a local inflammatory reaction that contributes to tissue damage. Microglial cells in particular become activated and provoke tissue injury by releasing pro-inflammatory mediators and reactive oxygen species (ROS). When oxygen supply is limited during ischaemia, a calcium influx may activate phospholipase C, which results in a breakdown of membrane phospholipids, or may convert xanthine dehydrogenase to xanthine oxidase in the cerebral blood vessels leading to the formation of superoxide radicals and hydrogen peroxide.

ROS causes oxidative damage that may affect lipids, proteins, nucleic acids and other molecules. Quantification of lipid peroxidation end products is considered to be a measure of whole-body oxidative damage. Serum malondialdehyde (MDA), a marker of lipid peroxidation, is the most abundant aldehyde generated by the attack of free radicals on polyunsaturated fatty acids of cell membranes; its measurement provides information of oxidative injury in vivo. The impact of free radicals may also be obtained by comparisons of antioxidant concentrations, because serious damage by free radicals implies insufficiency of the body’s multilevel defence systems against radicals. Measurement of the total antioxidant capacity (TAC) of biological fluids, however, is regarded as more physiologically representative in certain settings than individual antioxidants, and is believed to be a useful measure of how much the antioxidants present can protect against oxidative damage to membranes and other cellular components.

C-reactive protein (CRP) has been the most extensively studied marker of inflammation. It is a novel plasma marker of atherothrombotic disease. C-reactive protein (CRP) is produced not only by the liver but also in atherosclerotic lesions by vascular smooth muscle cells and macrophages in response to stimulation by the ‘pro-inflammatory’ cytokine interleukin-6 (IL-6). Elevated plasma levels of CRP are not disease specific but are sensitive markers which are produced in response to tissue injury, infectious agents, and inflammation.

Various cross-sectional studies support the notion that CRP may be a marker for stroke and post-stroke status. Several studies support the role of CRP in the prediction of ischaemic stroke risk and outcome, as well as the possible role of inflammation before and after stroke. As the methods traditionally employed to measure CRP do not have good sensitivity, measurement of highly-sensitivity C-reactive protein (hsCRP) is recommended to evaluate atherothrombotic disease, which usually presents with lower CRP levels than the other inflammatory processes.

Ginkgo biloba extract (EGb 761) is known to have neuroprotective properties in diseases associated with free radical generation. Extensive studies on G. biloba extracts showed their ability to protect brain neurons from oxidative stress and to inhibit apoptosis in cell culture. The G. biloba extracts that are currently used for medicinal purposes contain 24% flavonoid glycosides (quercetin, kaempferol, isorhamnetin) and 6% terpene lactones (ginkgolides A, B, C, M, J and bilobalides). The EGb 761 components eliminate free radicals...
such as the hydroxyl radical and the superoxide anion. Quercetin is a powerful antioxidant in the flavonoid family due to its molecular configuration, which is capable of eliminating free radicals. The pharmacologically active terpene lactones selectively inhibit the platelet-activating factor, preventing thrombus formation. Bilobalide is reported to possess neuroprotective properties.

The aim of the present study was to investigate the presence of oxidative stress and inflammation in serum samples of ischaemic stroke patients by measuring MDA concentrations, total antioxidant status (TAS), and hsCRP in the early post-ischaemic period, and to determine the role of G. biloba therapy in correcting the markers of oxidative stress and inflammation in question.

### Methods

This double-blind randomised study was conducted in the Ibn Seena Hospital, Department of Neurology, in Mosul City, from January 2009 to April 2011. Approval was obtained from the ethical committee of the main health centre in Nineveh in Mosul City and the College of Medicine University of Mosul, Iraq. Our study included 31 CVA hypertensive patients (26 males and 5 females) suffering from ischaemic stroke, aged 69.03 ± 2.96 years and 30 healthy control subjects aged 69.40 ± 2.69 years.

All patients included in this study were initially diagnosed as having CVA, or acute ischaemic stroke. All had problems with anterior circulation, a diagnosis made on the basis of full physical and neurological examinations by a neurologist. The diagnoses were then confirmed by either a magnetic resonance imaging (MRI) or computed tomography (CT) scan of the brain. Vascular risk factors including hypertension or diabetes mellitus, and smoking and alcohol habits were recorded. Patients with haemorrhagic stroke, intracranial tumour, or other neurological diseases, infection, inflammation, liver disease, and renal failure were excluded. For controls, the criteria were as follows: age ≥60 years, healthy subjects, non-smokers, and not taking vitamin supplements.

Ischaemic stroke patients were divided into two groups: group I (n = 15 of a possible 18 patients) included patients with ischaemic stroke who received conventional therapy (aspirin, rosuvastatin and lisinopril), and group II (n = 16 of a possible 28 patients) included patients who received conventional therapy with G. biloba (1500 mg/day) for 30 days. The dose was decided as a safe increment after previous promising results with 500 and 1000 mg/day.

Blood samples were initially obtained from all CVA patients within 48–120 hours of their accidents, and before starting treatment. They were also taken from the controls. Assays of the serums MDA, TAS and hsCRP were done at the Department of Pharmacology in the College of Medicine at the University of Mosul. For the patient group, another blood sample was taken after treatment with either conventional therapy or conventional therapy with G. biloba, and the parameters reassessed.

MDA was measured by the method outlined by Buege and Aust where MDA reacts with thiobarbituric acid (TBA) to yield a red-coloured product. The absorbance of a 3 ml coloured layer was measured at 535 nm spectrophotometrically. TAS was measured by peroxidase/H₂O₂/ABTS colorimetric assay using commercial kits from Randox Laboratories, Belfast, UK. CRP was measured using the BioCheck hsCRP ELISA Kit (BioCheck, Inc., Foster City, California, USA).

Data were expressed as means ± standard deviation (SD). Statistical comparisons were performed using the Student’s t-test between patients before therapy and controls, and the one-way analysis of variance (ANOVA). The Dunnett test was used to compare groups of patients. Linear regression analysis and Pearson correlation coefficients (r) were performed to determine the relationships between parameters. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows (Version 11.5, Chicago, Illinois, USA). A P value of

### Table 1: Concentrations of malondialdehyde (MDA), total antioxidant status (TAS), and highly-sensitivity C-reactive protein (hsCRP) in patients with acute ischaemic stroke before therapy and in healthy controls

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control (n = 30)</th>
<th>Ischaemic stroke patients before therapy (n = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDA (µmol/L)</td>
<td>1.03 ± 0.17</td>
<td>2.11 ± 0.28***</td>
</tr>
<tr>
<td>TAS (mmol/L)</td>
<td>1.85 ± 0.12</td>
<td>1.06 ± 0.13***</td>
</tr>
<tr>
<td>hsCRP (mg/L)</td>
<td>0.53 ± 0.09</td>
<td>1.79 ± 0.18***</td>
</tr>
</tbody>
</table>

Notes: Results are expressed as mean ± SD; *** Significant difference from control at P ≤0.001
Oxidative Stress and C-Reactive Protein in Patients with Cerebrovascular Accident (Ischaemic Stroke)

The role of Ginkgo biloba extract

<0.05 was considered statistically significant.

**Results**

The serum levels of MDA, TAS and hsCRP from healthy subjects and patients with acute ischaemic stroke before starting drug therapy are shown in Table 1. The serum levels of MDA and hsCRP were found to be significantly higher ($P \leq 0.001$) and TAS were significantly lower in ischaemic stroke patients in the early post-ischaemic period (before starting therapy) in comparison to the controls [Table 1].

Table 2 shows the serum levels of MDA, TAS, and hsCRP in the two groups of ischaemic stroke patients before and after therapy. Patients in group I reported a significant reduction in serum levels of MDA ($P \leq 0.001$) and hsCRP ($P \leq 0.01$), and a significant increase ($P \leq 0.01$) in serum levels of TAS after treatment with conventional therapy in comparison with their levels before therapy.

Also, patients in group II reported a significant reduction in serum levels of MDA ($P \leq 0.001$) and hsCRP ($P \leq 0.001$) and a significant increase in serum levels of TAS ($P \leq 0.001$) after treatment with *G. biloba* together with conventional therapy in comparison with their levels before therapy.

By comparing the serum levels of MDA, TAS, and hsCRP between the two groups of ischaemic stroke patients after therapy, no significant differences ($P = 0.19$) were reported in serum MDA levels between group I, who received conventional therapy, and group II, who received *G. biloba* with conventional therapy, whereas the serum levels of TAS were found to be significantly higher ($P \leq 0.01$) and hsCRP were significantly lower ($P \leq 0.01$) in group II who received *G. biloba* with conventional therapy in comparison with group I who received conventional therapy alone [Table 2].

Regarding correlations between different biochemical parameters, Figures 1 to 3 show the relationships between MDA, TAS, and hsCRP in patients with acute ischaemic stroke. A significant negative correlation ($r = -0.418$, $P = 0.001$) was observed between MDA and TAS in the serum samples of patients with acute ischaemic stroke. MDA had a significant positive correlation with hsCRP ($r = 0.729$, $P \leq 0.001$), and there was a significant negative correlation ($r = -0.602$, $P < 0.001$) between TAS and hsCRP in the serum samples of ischaemic stroke patients.

**Discussion**

There is strong indirect evidence that free radical production appears to be an important mechanism of brain injury after exposure to ischaemia and reperfusion. Free radicals in biological samples are difficult to measure because they are extremely reactive and have a short half-life. Therefore, particularly in human studies, indirect approaches have been used to demonstrate free radical production during cerebral ischaemia by measuring the products of free radical reaction with other molecules, such as lipids, proteins, and deoxyribonucleic acid (DNA), and the level or activity of antioxidant molecules. ROS causes impairment of cellular membrane stability and cell death by lipid peroxidation. MDA is the end product of the lipid peroxidation process. An increase in free radicals causes overproduction of MDA, which is commonly known as a marker of oxidative stress.

### Table 2: Concentrations of malondialdehyde (MDA), total antioxidant status (TAS), and highly-sensitivity C-reactive protein (hsCRP) in patients with acute ischaemic stroke before therapy and after therapy

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group I (n = 15)</th>
<th>Group II (n = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before therapy</td>
<td>After conventional therapy</td>
</tr>
<tr>
<td>MDA (µmol/L)</td>
<td>2.12 ± 0.26</td>
<td>1.98 ± 0.24***</td>
</tr>
<tr>
<td>TAS (mmol/L)</td>
<td>1.07 ± 0.12</td>
<td>1.15 ± 0.12**</td>
</tr>
<tr>
<td>hsCRP (mg/L)</td>
<td>1.80 ± 0.17</td>
<td>1.69 ± 0.20**</td>
</tr>
</tbody>
</table>

Notes: Results are expressed as mean ± SD; ** Significant difference compared to before therapy at $P \leq 0.01$ and *** at $P \leq 0.001$; δδ Significant difference compared to after conventional therapy at $P \leq 0.01$.
In the present study, it was observed that ischaemic stroke patients in the early post-ischaemic period (before starting therapy) had significantly higher levels of serum MDA and hsCRP, and significantly lower TAS than controls. These findings provide evidence for the presence of oxidative stress and inflammation in ischaemic stroke patients.

There are several possible reasons for increased lipid peroxidation in cases of ischaemic stroke. First, the brain’s cellular membranes are very rich in polyunsaturated fatty acid side chains, which are especially sensitive to free radical attack. Additionally, they have a low content of antioxidant enzymes, such as catalase and glutathione peroxidase, while the brain contains a significant amount of iron, despite the fact that its iron binding capacity is not very high. Iron ions are known to stimulate free radical generation.32,33 Lower TAS was accounted for by an increased use of endogenous antioxidants to fight free radicals and oxidative stress during ischaemic stroke.34

Our findings are in accordance with several studies which have been done to evaluate oxidative stress, antioxidant status, and markers of inflammation in ischaemic stroke patients.5-8 Most of these studies have shown enhanced levels of oxidative stress which are markers of inflammation, and reduced levels of antioxidants;5,10 however, some studies have reported controversial and conflicting results with regard to the levels of antioxidant enzymes.35

Studies evaluating markers of oxidative stress in patients in the early period of ischaemic stroke revealed an increase in the blood, cerebrospinal fluid, or salivary concentrations of lipid peroxides, protein carbonyl, homocysteine, nitric oxide, and of MDA, conjugated dienes, and other TBA-reactive molecules at the onset of stroke.3,10,33,36-39 Some studies showed persistently elevated MDA concentrations 6 months after strokes.40

Evaluations of antioxidants in blood, urine, or cerebrospinal fluid of ischaemic stroke patients revealed lower plasma vitamin C, E, vitamin A, and uric acid, lower glutathione peroxidase (GPX) activity, decreased glutathione (GSH) concentration, and a decreased total plasma antioxidant capacity.8,10,32,34,35,37,41 Data associated with superoxide dismutase (SOD) activity after acute ischaemic stroke are controversial. SOD activity of patients with acute ischaemic stroke was reported to be reduced in the serum and increased in the cerebrospinal fluid (CSF), increased in both CSF and serum, or remained unchanged.32,24,43

Several prospective studies have shown that an elevated serum CRP concentration is a strong predictor of cardiovascular events, including stroke. CRP plays an important role as a marker of outcome and may determine the degree of recovery for stroke patients.

In their study, Sánchez-Moreno et al. found that ischaemic stroke patients had significantly

**Figure 1:** The relationship between malondialdehyde (MDA) and total antioxidant status (TAS) in patients with acute ischaemic stroke ($r = -0.418$, $P = 0.001$)
Oxidative Stress and C-Reactive Protein in Patients with Cerebrovascular Accident (Ischaemic Stroke)

The role of Ginkgo biloba extract elevated markers of inflammation, marked by CRP, intracellular adhesion molecule-1 (ICAM-1), and chemokine monocyte chemottractant protein-1 (MCP-1), and that elevated CRP concentrations were associated with a two-fold increase in the risk of ischaemic stroke. Winbeck et al. observed that an increase in CRP levels between 12 and 24 hours after the onset of symptoms predicts an unfavorable outcome and is associated with an increase in the incidence of cerebrovascular events. Mishra et al. observed an increase in hsCRP levels in stroke patients and that the increased levels were correlated with larger infarct, severe neurological deficit, and worse outcomes.

Our study showed a highly significant negative correlation between serum MDA levels and TAS in ischaemic stroke patients, which suggests increased utilisation by ROS as an important contributing factor to the lower concentrations of antioxidants in ischaemic stroke patients.

In the present study, we have investigated the relationship between markers of oxidative stress and markers of inflammation in ischaemic stroke patients. Ischaemic stroke patients with higher serum hsCRP concentrations, indicative of greater inflammatory response, also had higher serum MDA levels and lower TAS than those with lower serum hsCRP concentrations. This can be observed in the figures, which show that serum hsCRP levels positively correlate with lipid peroxidation products and negatively correlate with TAS.

Our findings are in accordance with Sánchez-Moreno et al.’s results in which they found that CRP were inversely associated with concentrations of antioxidant vitamins C and E, and positively associated with markers of oxidative stress (8-isoprostanes).

This study also showed that patients in groups I and II reported a significant reduction in serum levels of MDA and hsCRP and a significant increase in serum levels of TAS after treatment in comparison with their levels before therapy.

Interestingly, we did not observe any statistically significant differences in serum MDA levels between group I, who received conventional therapy, and group II, who received G. biloba with conventional therapy. In fact, the serum levels of TAS were found to be significantly higher, while those of hsCRP were significantly lower in group II who received G. biloba with conventional therapy, in comparison with group I who received conventional therapy alone.

Higher TAS in the serum of ischaemic stroke patients who received G. biloba together with conventional therapy (group II) was most likely caused by a lower use of endogenous antioxidants because of supplementary antioxidant effects of flavonoids glycosides.

Antioxidant treatment may be an efficient therapeutic option for cardiac embolisms and macroangiopathic strokes, contributing to an improvement of neurological deficits and the functional status of the patients through the reduction of oxidative stress following ischaemia.

Figure 2: The relationship between malondialdehyde (MDA) and highly-sensitivity C-reactive protein (hsCRP) in patients with acute ischaemic stroke ($r = 0.729, P < 0.001$)
It has been reported in many studies that G. biloba improved tissue damage in various organs through its antioxidant effect. Zeybek et al. reported that G. biloba significantly decreased MDA levels and histopathological scores of the pancreatitis in rats. Bridi et al. reported that G. biloba had antioxidant activity in the hippocampus, striatum, and substantia nigra of rats. EGb 761 has an antioxidant effect as a free radical scavenger, a relaxing effect on vascular walls, an ameliorating effect on blood flow and microcirculation, and a stimulating effect on neurotransmitters. Besides a direct scavenging effect on ROS, G. biloba exerts an anti-inflammatory effect on inflammatory cells by suppressing the production of ROS and nitrogen species.

Several studies have shown that EGb 761 could protect cultured neurons against damage induced by peroxynitrate and hydrogen peroxide. Zhang et al. demonstrated that total ginkgolides (TG) (a terpenoid constituent of EGb 761) protected cultured rat cortical neurons from oxidative damages induced by hydrogen peroxide (H₂O₂).

EGb 761 extract, with free radical scavenging activity, has been shown to reduce the size of cerebral infarction and improve neurological behaviour in rats with permanent and transient mid-cerebral artery occlusion (MCAo).

Saleem et al. showed that the standardised EGb761 significantly improved the outcome in mice after cerebral ischaemia and reperfusion in terms of neurobehavioral function and infarct size without affecting physiological parameters.

Our findings suggest a potential role of G. biloba in acute ischaemic stroke, and the findings are important in view of the fact that stroke is, at present, the third leading cause of death worldwide. The mechanisms by which G. biloba normalise the cerebral damage, and reduce oxidative stress and inflammation, can probably be attributed to the antioxidant effects of flavonoids combined with the anti-inflammatory properties of the terpenoids bilobalide and ginkgolides A, B, C, M, J, and the terpenoids antagonists of platelet-activating factor (PAF), making this natural extract plausible to use in the treatment of ischaemic stroke, which is characterised by both oxidative damage and inflammation.

One of the limitations of this study is that it does not relate the biochemical changes to the clinical evaluation and outcome prognosis.

**Conclusion**

From this study, we conclude that acute ischaemic stroke is associated with oxidative stress and inflammatory response as indicated by increased lipid peroxidation products (MDA), reduced TAS and elevated levels of hsCRP in the early post-ischaemic period, and that G. biloba therapy has a potential role in reducing oxidative damage and inflammatory response in ischaemic stroke patients.
CONFLICT OF INTEREST
No funding was received for this study and the authors declared no conflict of interest.

References


Psychological Health of First-Year Health Professional Students in a Medical University in the United Arab Emirates

Kadayam G Gomathi, Soofia Ahmed, Jayadevan Sreedharan

Abstract: Objectives: The aim of this study was to assess the psychological health of first-year health professional students and to study sources of student stress. Methods: All first-year students (N = 125) of the Gulf Medical University (GMU) in Ajman, United Arab Emirates (UAE), were invited to participate in a voluntary, anonymous, self-administered, questionnaire-based survey in January 2011. Psychological health was assessed using the 12-item General Health Questionnaire. A 24-item questionnaire, with items related to academic, psychosocial and health domains was used to identify sources of stress. Pearson's chi-squared test and the Mann-Whitney U-test were used to analyze the data. Results: A total of 112 students (89.6%) completed the survey and the overall prevalence of psychological morbidity was found to be 33.6%. The prevalence of psychological morbidity was not significantly associated with any of the demographic factors studied. However, total stress scores and academics-related domain scores were significantly associated with psychological morbidity. Conclusion: Psychological morbidity was seen in one in three first-year students attending GMU. While worries regarding the future and parental expectations were sources of stress for many students, psychological morbidity was found to be significantly associated with only the total stress and the academic-related domain scores.

Keywords: Psychological stress; Medical student; Health professions; Undergraduate medical education; United Arab Emirates.
A university student’s life is subject to many different kinds of stress. Sources of student stress can be academic pressures, social or personal issues, and financial problems. In recent years, there has been a growing appreciation of the stresses involved in the training of health professionals. Several studies have shown stress among medical students and qualified doctors to be higher than that of the general population and other college students. Health professional students not only have to face the challenge of a rigorous curriculum, but also have to learn to deal with emotionally difficult experiences. The pressures put on students by academics, an obligation to succeed, the difficulties of integrating into the system, and social, emotional and family problems are all potential stressors which can affect learning ability and academic performance. High stress levels have been reported in not only medical, but also in dental, pharmacy and physiotherapy students from various parts of the world. Studies from Arab countries also indicate high stress levels in medical and dental students.

The Gulf Medical University (GMU) in Ajman, United Arab Emirates (UAE), is a 13-year-old international university where students from different cultures, educational backgrounds, and parts of the world study together. A large number of students are in the UAE for the first time. Many first-year students are adjusting not only to a new learning environment but also to a new culture during their training in GMU. Our objective was to assess the psychological health of the first-year health professional students and to study the various sources of psychological stress.

Methods
A cross-sectional survey using a voluntary, anonymous, self-administered questionnaire was carried out in January and February 2011, about five months after the first-year students had joined GMU. All 125 first year undergraduate students were contacted for the survey. This study was approved by the Ethics Committee of GMU. Participants were informed about the study, verbal consent was taken, and participation was voluntary and anonymous.

The questionnaire had three parts. The first part obtained demographic details. The second part of the questionnaire was the well-validated 12-item General Health Questionnaire (GHQ-12). The GHQ-12 method of scoring (0-0-1-1) was used. Scores were summed up to give a total score for each student, with a maximum possible score being 12. Based on the mean and median values, a cutoff score of 4/5 was considered appropriate. Students with scores of 0–4 were coded as having no or very few signs of possible mental health problems (i.e. were in normal psychological health [N]), while students with scores of 5 and above were determined to be GHQ-12 cases and to have psychological morbidity (PM).

Sources of stress were identified in the third part of the questionnaire, which was based on the studies by Sreeramareddy et al. and El-Gilany et al. It had 24 items grouped into three domains: academic-related, psychosocial, and health-related. It was developed with the help of experts in the field, checked for validity, and pilot tested before use. Students were asked to rate the frequency of occurrence of the stressor on the scale ‘never/rarely’, ‘sometimes’, or ‘often/always’. ‘Never/rarely’ and ‘sometimes’ were given a score of 0 and responses of ‘often/always’ were scored as 1. Negatively worded questions were reverse scored. Data were entered into the Predictive Analytics SoftWare (PASW)
Statistics software (Version 18, SPSS-IBM, Chicago, Illinois, USA) and analysed. Pearson’s chi-squared test and the Mann-Whitney U-test were used for testing significance.

Results

All 125 first year undergraduate students were contacted for the survey. Of that number, 112 students completed the survey, giving a response rate of 89.6%. The characteristics of the participants are given in Table 1.

The students’ psychological health is shown by the distribution of the GHQ-12 scores in Figure 1. The mean ± standard deviation (SD) of the GHQ-12 score was 3.53 ± 2.57, while the median GHQ-12 score was 3.0.

Using the GHQ-12 and a cutoff of 4/5, the prevalence of psychological morbidity was found to be 33.6% in the first-year undergraduate students at GMU.

As shown in Table 1, more psychological morbidity was seen in female students (36.6%) as compared to male students (30.8%). Psychological morbidity was also found to vary among students in the different programs. Morbidity was higher (40.6%) in students with other languages of instruction in high school compared to those who had been taught in English (31%). However, psychological morbidity was not found to be significantly associated (P >0.05) with any of the demographic groups studied.

| Table 1: Demographic variables and psychological health of the students |
|-------------------------|------------------|------------------|------------------|
| Variable*               | Group            | Normal Number (%)| Psychological Morbidity Number (%)| Total Number |
| Gender                  | Female           | 46 (63.4)        | 27 (36.6)        | 73            |
|                         | Male             | 27 (69.2)        | 12 (30.8)        | 39            |
| Programme               | MBBS             | 28 (60.9)        | 18 (39.1)        | 46            |
|                         | DMD              | 20 (69)          | 9 (31)           | 29            |
|                         | Pharm D          | 14 (73.7)        | 5 (26.3)         | 19            |
|                         | BPT              | 12 (66.7)        | 6 (33.3)         | 18            |
| Marital status          | Unmarried        | 64 (66)          | 33 (34)          | 97            |
|                         | Married          | 10 (66.7)        | 5 (33.3)         | 15            |
| Language of instruction in high school | English | 55 (68.8)       | 25 (31.3)        | 80            |
|                         | Other            | 19 (59.4)        | 13 (40.6)        | 32            |
| Accommodation           | Living alone (hostel/apartment) | 37 (69.8)      | 16 (30.2)        | 53            |
|                         | Living at home   | 37 (62.7)        | 22 (37.3)        | 59            |
| Family details          | Parents living together | 60 (64.5)      | 33 (35.5)        | 93            |
|                         | Parents separated/divorced| 14 (73.7)    | 5 (26.3)         | 19            |
| Parent(s) in a health-related profession | Yes        | 21 (67.7)        | 10 (32.3)        | 31            |
|                         | No               | 53 (65.4)        | 28 (34.6)        | 81            |
| On financial aid/scholarship | Yes           | 7 (87.5)         | 1 (12.5)         | 8             |
|                         | No               | 67 (64.4)        | 37 (35.6)        | 104           |
| Self-reported academic performance | Satisfactory | 27 (67.5)       | 13 (32.5)        | 40            |
|                         | Unsatisfactory  | 47 (32.5)        | 25 (67.5)        | 72            |

Legend: MBBS = Bachelor of Medicine, Bachelor of Surgery; DMD = Doctor of Dental Medicine; Pharm D = Doctorate in Pharmacy; BPT = Bachelor of Physiotherapy
*None of the variables were found to be significantly associated with psychological morbidity
The stressors were classified into three domains: academic-related, psychosocial and health-related. In the academic-related domain, the total student population identified the following as ‘often’ or ‘always stressful’: ‘frequency of exams’ (22%), ‘academic workload’ (19%), and ‘time management’ (19%). In the psychosocial domain, the main concerns were ‘worries regarding future’ (50.5%), ‘high parental expectations’ (45%), ‘anxiety’ (21%) and ‘dealing with members of the opposite sex’ (18%). Getting along with peers, loneliness, and financial or family problems were identified as stressors by less than 10% of the students. Among the health-related issues, ‘irregular eating habits’, ‘lack of exercise’, and ‘lack of a healthy diet’ were reported as ‘often’ or ‘always stressful by 39%, 35% and 22.5% of the total student population, respectively. Sleep-related problems were a concern for 25% of the students. Illness and tobacco/alcohol abuse were identified as stressors by only 6 and 4 students, respectively.

Table 2 compares the percentage of students in the normal and psychologically morbid groups reporting academic-related, psychosocial, and health-related stressors. Within the academic-related domain, only ‘satisfaction with lectures/classes’ and ‘ability to concentrate’ were negatively associated with psychological morbidity (P <0.05). In the psychosocial domain, ‘family problems’ were found to be significantly associated with psychological morbidity, while in the health-related domain, ‘lack of regular eating habits’ was associated with significantly more students in normal health compared to those with psychological morbidity. Between the two groups, none of the other stressors were found to be statistically different.

A total stress score and stress scores in each of the three domains were generated for each student. The median total stress score of the psychological morbidity group was 5 while that of the normal group was 4. This difference was statistically significant (P <0.05). Among the three domains, only the median academic-related domain score was significantly different (P <0.05) between the students in normal psychological health (0) as compared to those having psychological morbidity (2).

Discussion
Stress is a physical, mental, or emotional response to events that causes bodily or mental tension. In small amounts, stress is normal and can help us be more active and productive. However, very high levels of stress experienced over a prolonged period can cause significant mental and physical problems.

GMU has a very diverse student population with students of 35 different nationalities coming from 15 different educational systems studying in the university. Adjusting to a new country, culture, educational system, along with being away from home for the first time, can cause significant amounts of stress. Since students join GMU after high school, most of the students in the first year are very young, with 92% being less than 21 years old. Female students outnumber male students; this is a trend that can be seen in all healthcare-related programmes at all universities in the UAE. About 29% of first-year students have studied science in a language other than English in high school, usually in Arabic or Persian. None of the students work part-time due to UAE laws. Very few students receive financial aid or scholarships, with most supported by their families.

Using the GHQ-12, the prevalence of psychological morbidity was determined to be 33.6% in first-year students. This prevalence, although high, is lower than that seen in medical students from the UK (36%), Iran (40%), or Malaysia (46%); however, it is higher than that reported from Nepal (20.9%), and lower than that reported in dentistry.
students from Jordan (70%) and Iraq (51%).\textsuperscript{12,13} We could not find any statistically significant difference in the prevalence of psychological morbidity between the genders [Table 1]. Conflicting reports are available in the literature, with some reporting a higher prevalence of psychological distress in females while others have reported no gender differences.\textsuperscript{1,2} There was no significant difference in the prevalence of psychological morbidity among students studying in different programmes at GMU. Some studies have reported higher stress levels in dentistry students compared to medical students while others have found higher levels of stress in medical students as compared to other health-related professions.\textsuperscript{22–23} The prevalence of psychological morbidity was higher in students who had studied in a language other than English at school compared to those who had studied in English [Table 1]. This observation, though not found to be statistically significant, correlates well with the higher percentage of students reporting ‘difficulty in reading textbooks’ in the psychological

Table 2: Percentage of students identifying stressors in the normal health and psychological morbidity group

<table>
<thead>
<tr>
<th>Type of stressor</th>
<th>Percentage of Students</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal Health (n = 73)</td>
</tr>
<tr>
<td><strong>Academic</strong></td>
<td></td>
</tr>
<tr>
<td>Academic workload too much</td>
<td>15.1</td>
</tr>
<tr>
<td>Satisfied with classes</td>
<td>97.3</td>
</tr>
<tr>
<td>Too frequent examinations</td>
<td>17.8</td>
</tr>
<tr>
<td>Satisfied with performance in examination</td>
<td>87.7</td>
</tr>
<tr>
<td>Learning material available</td>
<td>90.4</td>
</tr>
<tr>
<td>Difficulty reading textbooks</td>
<td>12.3</td>
</tr>
<tr>
<td>Able to manage time</td>
<td>84.9</td>
</tr>
<tr>
<td>Able to concentrate</td>
<td>94.5</td>
</tr>
<tr>
<td><strong>Psychosocial</strong></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>17.8</td>
</tr>
<tr>
<td>Parental expectations too high</td>
<td>42.5</td>
</tr>
<tr>
<td>Worries about future</td>
<td>52.1</td>
</tr>
<tr>
<td>Problems adjusting to classmates</td>
<td>9.6</td>
</tr>
<tr>
<td>Loneliness</td>
<td>8.2</td>
</tr>
<tr>
<td>Financial problems</td>
<td>4.1</td>
</tr>
<tr>
<td>Family problems</td>
<td>1.4</td>
</tr>
<tr>
<td>Difficulty getting along with members of the opposite sex</td>
<td>20.5</td>
</tr>
<tr>
<td>Lack of recreation</td>
<td>30.1</td>
</tr>
<tr>
<td><strong>Health-related</strong></td>
<td></td>
</tr>
<tr>
<td>Lack of healthy diet</td>
<td>23.3</td>
</tr>
<tr>
<td>Irregular eating habits</td>
<td>45.2</td>
</tr>
<tr>
<td>Sleep problems</td>
<td>21.9</td>
</tr>
<tr>
<td>Illness/health problems</td>
<td>2.7</td>
</tr>
<tr>
<td>Tobacco/alcohol/substance abuse</td>
<td>1.4</td>
</tr>
<tr>
<td>Lack of exercise</td>
<td>39.7</td>
</tr>
</tbody>
</table>

*Significant difference between the two groups (P <0.05)
morbidity group [Table 2]. Even though the Test of English as a Foreign Language (TOEFL) is a mandatory requirement for admission into GMU, students who have studied in Arabic or Persian in high school often find it difficult to keep up with reading assignments in the first year. These findings are similar to the difficulty in reading textbooks and the translation of English terms reported by 44.8% of students from a medical college in Egypt where most of the students had studied in Arabic in high school, as well as the anecdotal references in a study from Saudi Arabia.24,28

The total stress score was found to be significantly associated with psychological morbidity. Though academic-related stressors were concerns for fewer students than psychosocial or health-related issues, a significant difference was found between the median academics-related domain stress scores of normal students and those with psychological morbidity. This also correlates well with the finding that significantly more students with psychological morbidity were dissatisfied with lectures/classes and were unable to concentrate in classes [Table 2]. These findings are similar to those reported in literature where stress in medical students was found related to academic training rather than personal factors.8,25 While similar proportions of self-reported unsatisfactory academic performance were found in healthy students and those having psychological morbidity [Table 1], it is interesting to note that among those with self-reported unsatisfactory academic performance, 67.5% had psychological morbidity, which correlates well with the significantly higher academic domain stress scores in students with psychological morbidity.

In the psychosocial domain, about half the student population reported often or always worrying about the future. This was surprising considering that these students had just entered the university and joined a professional programme. ‘High parental expectations’ was also a cause of stress for 45% of the student population. This finding is similar to that reported from Asian countries like Nepal and Pakistan where ‘high parental expectations’ were a cause of stress for 52 and 63% students, respectively.18,26 In this context, it is also interesting to note that there was a significant association between family problems and psychological morbidity [Table 2]. Dealing with members of the opposite sex was reported as stressful by 18% of the students. This was not unexpected since GMU is one of the few universities in the UAE with mixed gender classes. Most high school students in Arab countries study in single gender schools and young people do not have much interaction with members of the opposite sex in academic or social settings. Similar findings have been reported in a recent study from Australia where Saudi international students transitioning from a single gender to a mixed gender environment experienced stress.27

Anxiety is an issue for many students (21%), but making friends at GMU does not seem to be a problem for most students as difficulty in getting along with peers and loneliness were concerns for less than 10% of the students. This is very encouraging since adjusting to a new environment is much easier if students can make friends. Since most of our students are supported by their families, financial problems were identified as a concern by less than 10% of the students.

Lack of recreation was identified as a stressor by 25% of the students. GMU is located in a small emirate in the UAE and affords few avenues for entertainment. Further, most students do not find time or opportunities to pursue their hobbies as is true for students in health-related professional training around the world.25

In the health-related domain, the lack of a healthy diet and irregular meals were reported by many students. Young adults, especially those living away from home, often do not eat at regular times or eat healthily, so this is not unexpected. It is encouraging to note that they are aware that they are not practicing healthy lifestyles. Sleep-related problems were a concern for 1 in 4 students. This is significant and is similar to reports in literature regarding sleep problems in medical students and needs to be addressed.26–30 Illnesses and tobacco/alcohol abuse were reported by only 6 and 4 students, respectively. This is a small percentage of the student population, but is not unexpected since the UAE is an Islamic country with strict rules regarding alcohol consumption, and most of the first-year students are very young.

This study has some limitations. All data obtained was self-reported, including academic performance, so the results need to be interpreted with care. It is possible that some students might have been in denial about certain issues or, due to
cultural reasons, were not able to answer certain questions truthfully. The study was a cross-sectional survey taken midway through the first year and may not be representative of student behaviours over time. The conclusions drawn are based on the data obtained from GMU and may not be applicable to other universities. We did not study the psychological health of other university students in the UAE for comparison.

Conclusion

In the first year of undergraduate studies at GMU, one in three students had psychological morbidity when screened using the GHQ-12. There was no significant difference in psychological morbidity between the genders. High parental expectations and worries about the future were sources of stress for about half the students. Anxiety, sleep-related issues, lack of recreation, and poor eating habits were also reported by many students. Total stress was significantly associated with psychological morbidity, highlighting the need for measures to reduce stress in students. While academic-related sources of stress were significantly associated with psychological morbidity, no such associations were seen for the psychosocial or health-related sources of stress.

ACKNOWLEDGEMENTS

We thank the students and the GMU authorities for their cooperation. We also wish to thank Dr. Sondus Al Omar, of the Department of Physiology at GMU, and Mrs Hina Aman, career counsellor, for their valuable suggestions during questionnaire preparation. We thank GL Assessment, UK, for permission to use the GHQ-12.

CONFLICT OF INTEREST

This study was carried out in the Gulf Medical University, Ajman, UAE, in January-February 2011 and was a non-funded study. None of the authors has any conflict of interest.

References


Assessment Methods of an Undergraduate Psychiatry Course at a Saudi University

Mostafa Amr* and Tarek Amin

Abstract: Objectives: In Arab countries there are few studies on assessment methods in the field of psychiatry. The objective of this study was to assess the outcome of different forms of psychiatric course assessment among fifth year medical students at King Faisal University, Saudi Arabia. Methods: We examined the performance of 110 fifth-year medical students through objective structured clinical examinations (OSCE), traditional oral clinical examinations (TOCE), portfolios, multiple choice questions (MCQ), and a written examination. Results: The score ranges in TOCE, OSCE, portfolio, and MCQ were 32–50, 7–15, 5–10 and 22–45, respectively. In regression analysis, there was a significant correlation between OSCE and all forms of psychiatry examinations, except for the MCQ marks. OSCE accounted for 65.1% of the variance in total clinical marks and 31.5% of the final marks, while TOCE alone accounted for 74.5% of the variance in the clinical scores. The results of this study revealed that there was no significant difference in the students' scores that correlated with gender differences. The objective structured clinical examination (OSCE) as a method of student assessment accounted for a sizable part of the variance in the clinical scores. The objective structured clinical examination (OSCE) as a method of student assessment accounted for a sizable part of the variance in the clinical scores. Conclusions: This study demonstrates a consistency among the students' assessment methods used in the psychiatry course, particularly in the clinical component, in an integrated manner. This information would be useful for future developments in undergraduate teaching.

Keywords: Undergraduate medical students; Assessment; Psychiatry; Undergraduate; Saudi Arabia.

Advances in Knowledge

- In Arab countries there are few studies on assessment methods in the field of psychiatry, so this study contributes new information.
- The results of this study revealed that there was no significant difference in the students' scores that correlated with gender differences.
- The objective structured clinical examination (OSCE) as a method of student assessment accounted for a sizable part of the variance in total clinical and final marks, which indicated that the implementation of OSCE is a useful adjunct to other forms of clinical assessment.

Applications to Patient Care

- This study showed that different forms of psychiatric assessment can improve student knowledge and the quality of their practice, and fulfill unmet information needs at the point of patient care.
- Students should be encouraged to become familiar with updated methods of assessment in psychiatry courses.
In Saudi Arabia, the College of Medicine at King Faisal University offers a six-year medical curriculum to selected Saudi students who have successfully completed one year of requisite general university studies following secondary school education. The first four years of the curriculum are devoted to pre-clinical (medical sciences and family medicine) learning. Students are exposed to behavioural sciences in the third year. In the fourth year, students are introduced to a problem-based learning (PBL) integrated curriculum. They practice communication, history taking, and the physical examination of different body systems, as well as relevant procedural skills. Training is conducted in a clinical skills laboratory using different types of simulators. They learn more about the interplay between the physical and psychological components of illnesses. The curriculum in years 5 and 6 is structured around a series of clerkship rotations in the departments of Internal Medicine, Surgery, Psychiatry, Obstetrics and Gynecology, and Pediatrics. Students graduate after successful completion of 12 semesters (229 hours per semester). The Department of Psychiatry attachment is a 6-week course based in a dedicated psychiatric hospital. Teaching-learning methods employed include lectures, small-group tutorials, and group discussions guided by department faculty. The major objectives of the Department for the attachment are that students 1) acquire a basic knowledge of the developmental aspects of psychiatric disorders; 2) identify and make use of all relevant sources of information when assessing each patient; 3) demonstrate competence in mental state examinations and physical assessments; 4) develop skills in appropriate communication with patients and colleagues, and 5) make a clear oral presentation of a case.

During the fifth year, students undertake six clinical rotations averaging 180 hours, arranged in two semesters of 3 rotations each. The group size for each rotation varies from 8 to 12 students. Since the Department was established in 2006, the rotating students have been evaluated through portfolios consisting of peer reviews, group work, case studies, ethics discussions, and critical reviews, and at the end of the course by a traditional oral clinical examination (TOCE) and an objective structured clinical examination (OSCE). At the end of the semester, a multiple choice question (MCQ) examination is held [Figure 1]. Furthermore, in 2009, the Psychiatry Department conducted a survey that assessed the students’ attitudes towards psychiatry that was published as an international education report. The survey showed favourable changes in the students’ attitudes following clerkship. However, less positive responses were seen in students’ attitudes towards the quality of the medical school clerkship.

To improve the student learning/assessment experience we introduced the OSCE for the summative assessment of students, in conjunction with a traditional oral examination and portfolio. The potential marks for the written paper, MCQ, portfolio, OSCE and clinical examination are 50, 10, 15 and 25, respectively, for a total of 100 points. Although the use of OSCEs in psychiatry has been described as less widespread than in other medical fields, recent years have witnessed an increased interest in its use in psychiatry. The objective of this study was to assess the outcome of different forms of psychiatric course assessment among fifth-year medical students at King Faisal University, Saudi Arabia.

Methods

This was a cross-sectional survey carried out during the 2010–11 academic year, in two consecutive semesters, in which cohorts of male and female students (54 and 56, respectively) were invited to participate in the study. All students agreed to participate in the study, which was approved by the college authorities.

The MCQ paper at each examination contained 50 items worth one mark each. The initial item bank of 500 questions was designed to cover the following content areas: causes/risks, signs/symptoms, course, treatments, and mental health services. Two items were included to represent each content area. One item was answered through simple recall, and the other was designed to be answered interpretatively and commonly involved a brief, one to four sentence case presentation. Each MCQ item consisted of a stem no longer than five sentences in length (though typically only 1–2 sentences), along with four response options. Test items were developed following standard, well-described MCQ writing procedures, and were designed to avoid ambiguity, vagueness, and value-
laden language. Reliability (Cronbach’s alpha) and concurrent validity (Pearson r) coefficients were obtained by correlating the scores of MCQ papers with the overall outcome of the examination. They were in the ranges of 0.83–.91 and 0.80–0.93 (P <0.05), respectively. Indices of item facility and discrimination were in the ranges of 50–91, and 0.37–.45, respectively.

In TOCE, to explore the student’s understanding of topics deemed relevant to curriculum, students interviewed and examined a real patient for over 45 minutes, and then summarised their findings to two examiners who questioned them by an unstructured oral examination on the patient’s problem. The student’s interaction with the patient was not observed. Reliability (alpha) and concurrent validity coefficients (Pearson r) were obtained by correlating the scores in the TOCE with the overall outcome of the examination. They were in the ranges of 0.58–.71 and 0.73–.81, respectively (P <0.05).

The OSCE was based on the curricular constructs that included six thematic topics: mood disorders, anxiety disorders, child psychiatry, psychosis, personality disorders, and substance abuse. A blueprint was developed for each OSCE to capture the clinical competencies in the covered topics. A map for the stations was devised to guide the examinees and organisers with clear written instructions to the examiners, patients, and examinees. The OSCE was composed of nine stations which included two manned stations. A manned station (MS) referred to a station that had a real patient and an examiner. Students were allowed 15 minutes to perform tasks at each station. The first station included a psychiatric interview, where students were to develop a rapport and conduct the interview within the assigned time frame for a male patient with schizophrenia. At the second station, the students assessed the mental status, with particular attention to the mood and affect, of a female patient with bipolar I mood disorder. In each station, two independent examiners rated the examinees independently according to checklists. The raters were selected from the lecturers who were not involved in the design and/or implementation of the station. Checklists contained the desired competencies to be examined (average 28 items). The scores were classified as ‘done’, ‘not done’, or ‘done incorrectly’, with questions on topics such as delusions, hallucinations, and performance. Each item was assigned a weight by the station’s authors. At the end of each checklist, there were 4 questions with a 3-point Likert scale addressing the interview technique and included factors like empathy, degree of coherence, and verbal and nonverbal expression. Following the MS, students moved to an unmanned station (UMS) (4 minutes each) which included four dependent data stations (4 minutes each) with questions based on the previously taken history or examination stations, and three independent data stations. In these independent stations, students read a poster giving information regarding a history/examination and/or investigations, and he/she was required to answer questions related to diagnosis, further investigations, or management. Students moved between stations on time keepers’ commands. Examiners supervised each station throughout the session and the whole group of students was assessed by a nearly identical process. At the end, the marking and answer sheets were
Table 1: Students’ scores along the different types of assessment in the psychiatry course, College of Medicine, King Faisal University.

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Total (N = 110)</th>
<th>Gender</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Females (n = 56)</td>
<td>Males (n = 54)</td>
<td></td>
</tr>
<tr>
<td>Written exam (50 marks)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>35.8 ± 4.2</td>
<td>35.9 ± 5.1</td>
<td>0.679</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>36.0</td>
<td>36.0</td>
<td></td>
</tr>
<tr>
<td>Minimum-maximum</td>
<td>22.0-45.0</td>
<td>28.0-42.0</td>
<td></td>
</tr>
<tr>
<td>Total clinical exam (50 marks)</td>
<td></td>
<td></td>
<td>0.143</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>42.0 ± 3.5</td>
<td>42.4 ± 3.7</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>42.0</td>
<td>43.5</td>
<td></td>
</tr>
<tr>
<td>Minimum-maximum</td>
<td>32.0-50.0</td>
<td>32.0-50.0</td>
<td></td>
</tr>
<tr>
<td>OSCE exam (15 marks)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>11.7 ± 1.5</td>
<td>11.9 ± 1.4</td>
<td>0.548</td>
</tr>
<tr>
<td>Median</td>
<td>12.0</td>
<td>12.0</td>
<td></td>
</tr>
<tr>
<td>Minimum-Maximum</td>
<td>7.0-15.0</td>
<td>9.0-15.0</td>
<td></td>
</tr>
<tr>
<td>TOCE exam (25 marks)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>21.7 ± 1.9</td>
<td>22.1 ± 1.9</td>
<td>0.059</td>
</tr>
<tr>
<td>Median</td>
<td>22.0</td>
<td>22.5</td>
<td></td>
</tr>
<tr>
<td>Minimum-Maximum</td>
<td>17.0-25.0</td>
<td>17.0-25.0</td>
<td></td>
</tr>
<tr>
<td>Portfolio (10 marks)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>8.6 ± 1.2</td>
<td>8.5 ± 1.4</td>
<td>0.872</td>
</tr>
<tr>
<td>Median</td>
<td>9.0</td>
<td>9.0</td>
<td></td>
</tr>
<tr>
<td>Minimum-Maximum</td>
<td>5.0-10.0</td>
<td>5.0-10.0</td>
<td></td>
</tr>
</tbody>
</table>

Legend: SD = Standard deviation; OSCE = objective structured clinical examination; TOCE = traditional oral clinical examination
* Mann Whitney test of significance.

Data analysis was carried out using the Statistical Software for the Social Sciences (SPSS) package (Version 15, Chicago, Illinois, USA). Median, mean, and standard deviations were calculated for examination marks. Statistical comparison was carried out using the Mann-Whitney test. Zero order and partial correlations were performed between test marks, and regression models were fitted to evaluate the predictive value of OSCE as an independent variable, either alone, or with other examinations, and total clinical score or total final marks as the dependent variables. To assess the reliability and credibility of the OSCE, statistical analyses of Cronbach alpha, Kappa, and Pearson’s correlation coefficient were used.

Results

Table 1 displays the students’ scores along the different assessment methods used to evaluate the outcome. The score range in the TOCE, OSCE, portfolio, and MCQ were 32–50, 7–15, 5–10 and
There was no significant difference in scores earned by different genders. A significant positive correlation was seen between OSCE and all forms of psychiatry examinations except for the written/MCQ marks [Table 2]. Strong positive correlations were found between components of the total clinical examination (especially TOCE and OSCE), while moderate correlations were found between TOCE and OSCE and low correlations with the portfolio (r = 0.86, 0.49 and 0.20, respectively). Figure 2 depicts the relationship between the students’ scores on the TOCE and written/MCQ examinations. There was no significant correlation between the two methods of assessment in students’ evaluations. On the contrary, Figure 3 shows a moderate and significant correlation between TOCE and OSCE (r = 0.493, P = 0.001).

The Kappa concordance coefficient and the correlation between the scores of examinees were computed. They ranged from 0.75 for station 1 to 0.64 for station 2. The Cronbach’s alpha coefficients for station 1 and 2 were 0.82 and 0.78, respectively. In the generated linear regression model, OSCE accounted for 65.1% of the variance in total clinical marks and 31.5% of the final marks (P = 0.001). One unit of change was associated with a 1.63 point change in the total clinical score and a 2.05 point change in final marks. In multiple regression analysis, the TOCE alone accounted for 74.5% of the variance in the clinical scores. Conditioned on its presence, the OSCE explained an extra variance of

Table 2: Correlation matrix between medical student scores in different examinations and total clinical scores (N = 110)

<table>
<thead>
<tr>
<th>Examinations</th>
<th>Pearson Correlation</th>
<th>Total clinical</th>
<th>OSCE</th>
<th>TOCE</th>
<th>Portfolio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written</td>
<td>r coefficient</td>
<td>0.162</td>
<td>0.157</td>
<td>0.154</td>
<td>0.020</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.091</td>
<td>0.102</td>
<td>0.108</td>
<td>0.835</td>
</tr>
<tr>
<td>Total clinical</td>
<td>r coefficient</td>
<td>--</td>
<td>0.807</td>
<td>0.863</td>
<td>0.558</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>--</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>OSCE</td>
<td>r coefficient</td>
<td>--</td>
<td>--</td>
<td>0.493</td>
<td>0.196</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>--</td>
<td>--</td>
<td>0.000</td>
<td>0.040</td>
</tr>
<tr>
<td>TOCE</td>
<td>r coefficient</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>0.379</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Legend: OSCE = objective structured clinical examination; TOCE = traditional oral clinical examination

22–45, respectively.
In regression analysis, the OSCE accounted for 65.1% of the variance in total clinical marks and 31.5% of the final marks ($P = 0.001$), while the TOCE alone accounted for 74.5% of the variance in the clinical scores.

**Discussion**

Findings from this study showed that the results of the MCQs are the most important predictors of final scores, as they accounted for 69.7% of student variability. These results are most likely due to the commonly observed relationship of a good quality MCQ test with other performance measures. It has been observed that general ability is the foundation of most performance measures and a well-constructed MCQ is the best estimator of this general ability.\(^5,6\) Also the results might reflect an unbiased evaluation of the medical students.\(^7\)

The acquisition of clinical skills is paramount to the development of a safe and competent practitioner.\(^8\) OSCE as a performance-based assessment is a well-established assessment tool for many reasons: it is a competency-based, valid, practical, and effective means of assessing clinical skills that are fundamental to the practice of medicine, and to other health care related professions.\(^9\) While OSCE is in use in many medical disciplines in Saudi Arabia, particularly in general surgery, orthopaedics and internal medicine, psychiatric educators have been slow to adopt this method of evaluation.\(^10-12\) To the best of the authors’ knowledge, this is the first report that addresses OSCE in undergraduate psychiatric assessment in Saudi Arabia. As expected, the implementation of OSCE in our Department has proved to be a useful adjunct to other forms of clinical assessment. The student’s scores on the OSCE correlated well with the results in clinical examinations and explained a great part of the variance in total clinical marks. Similar findings have been reported in different specialties from different countries;\(^13-15\) However, these studies did not show a correlation between the results of the OSCE and the MCQs. This may be attributed to the fact that MCQs assess the students’ cognitive abilities, covering the area of ‘knows’ and ‘knows how’ of Miller’s pyramid of assessment, and possibly spanning the levels of Bloom’s taxonomy of educational objectives, from the level of comprehension to the level of evaluation.\(^16\) Additionally, the OSCE, like other forms of clinical examinations, tests a different domain of clinical skills (covering the area of ‘shows how’ of the Miller’s pyramid of assessment) which is a prerequisite for physician performance in real life, such as history taking and physical examinations.\(^3\) Nonetheless, our results should be interpreted with caution as, according to previous studies in the literature, only two of the stations in our OSCE examination are considered classic OSCE stations.\(^3\)

The results of the study show that the most significant predictor of overall clinical scores is the TOCE. It alone explained 74.5% of the variance in clinical scores. Conditioned on the presence of the TOCE, the OSCE explained an extra variance of 19.2%. The examiners awarded high marks to favour a more pleasurable student-teacher encounter which unfortunately created a ‘halo effect’ in the evaluation of the students. The OSCE significantly correlates with the TOCE, but still has an important role in predicting total clinical marks. It explained 65.1% of the variance in total clinical marks. A better designed OSCE and external examiners in the TOCE would help to increase the accuracy and reliability of clinical assessment.

**Conclusion**

This study demonstrates that different clinical methods used to assess medical students during their Psychiatry course were consistent and integrated. This information would be useful for future developments in undergraduate teaching of this subject.

**Acknowledgements**

The authors would like to thank Dr. Feroze Kaliyadan, Assistant Professor of Dermatology at King Faisal University, for his assistance in revising the manuscript.

**Conflict of Interest**

No funding was received for this study, and no conflict of interest exists.

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B\n\nLUNT TRAUMA CAN CAUSE INJURIES TO a variety of intra-abdominal organs. Solid organ injuries are more common than intestinal perforations and are usually evident on presentation as these may be associated with varying degrees of shock or clinical signs of peritonitis. While perforation of the gastrointestinal tract is reported in 5–15% of patients, it may be difficult to diagnose at initial presentation, especially if signs of peritonitis are minimal. Studies vary regarding the most common site of intestinal perforation; however, there is a consensus that isolated jejunal blow out (IJBO) is extremely rare. Clinical presentation is usually delayed if the nature of the trauma is trivial. We report the case of a patient who presented with features of peritonitis 10 days after being injured by a knee kick trauma. An erect abdominal X-ray showed extraluminal air-fluid levels, suggesting a hollow viscous injury which on exploration was found to be IJBO.

Case Report

An 18-year-old male with no significant past medical or surgical history was brought to the emergency department 10 days after an incident of blunt trauma to the abdomen. The injury occurred when the patient swung from a great height and

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landed on his friend’s knee. This caused trauma to the epigastrium. The patient experienced sudden, severe abdominal pain, which settled after a while. No medical advice was sought for the problem; instead, for one week, the patient took over-the-counter medications for pain, including paracetamol 1 g PO (per os = by mouth) every 6 hours, and diclofenac sodium 50 mg PO b.i.d. (bis die = twice daily). After a few days, the pain became continuous. Over the following week, the patient started vomiting, and developed abdominal distension and absolute constipation. The patient’s condition worsened and he was brought to hospital, after experiencing altered mental states, with an unremitting fever, and decreased urine output.

Examination in the emergency department revealed a young adult in a state of shock with a pulse of 120 beats per minute, blood pressure of 90/60 mm Hg, a respiratory rate of 24 breaths per minute, a temperature of 38.8 °C, and an arterial oxygen saturation (SaO2) level of 95% at room air. He was not jaundiced but was extremely pale. A chest examination revealed equal air entry with no added sounds and a gallop rhythm on cardiac auscultation. An abdominal examination revealed distended rigid abdomen with guarding and rebound tenderness. Shifting dullness was positive and bowel sounds were absent. A digital rectal examination revealed an empty collapsed rectum. The patient was immediately resuscitated with supplemental oxygen via a face mask, and intravenous fluids and given antibiotics (metronidazole 500 mg at 8-hourly intervals and ceftriaxone 1 g every 12 hours). A nasogastric tube was inserted and urinary catheterisation was done to monitor output. Once the patient was stable, baseline investigations were undertaken which revealed a white blood count of 16,000 mm³ with neutrophilia of 75%; Hb levels of 6.206 g/L; blood urea levels of 28.6 mmol/L; serum creatinine levels of 132.6 μmol/L; potassium levels of 3.2 mmol/L, and abnormal liver enzymes and function, with a total bilirubin of 29 μmol/L, alanine transaminase (ALT) 60 μ/L, and aspartate transaminase (AST) 74 IU/L. His serum amylase level was 82 U/L. Radiological investigations yielded a normal chest X-ray, but an erect abdominal X-ray revealed a ground glass appearance, obscured psoas shadows, intraluminal air-fluid levels, free air under the right hemidiaphragm [Figure 1]. A computed tomography (CT) scan was not done as clinical pictures and X-ray findings were suggestive of perforation of a hollow organ which needed immediate surgical intervention.

The diagnosis of peritonitis due to a hollow viscous injury was made and an exploratory laparotomy was done. Findings included 3 litres of fluid containing pus and intestinal contents, and a single 1 x 1 cm perforation in the jejunum, 30 cm away from the duodeno-jejunal junction. Although the general condition of the patient was not good, primary repair of the perforation was done, after refreshing the margins, because of its proximal position. Extensive peritoneal lavage was done and the abdomen was closed by retention sutting. Recovery from anaesthesia was delayed and patient required observation in the intensive care unit for one night. Later he was moved to the ward. His progress in the ward was uneventful. He recovered very well and was discharged on day 10.

Discussion

Since Razali et al.5 published a report on isolated jejunal injury arising from blunt abdominal trauma in 1974, many other authors have reported such injuries.6–11 Even so, the total number of reported cases of IJBO in literature is not very high.12 The causes of injury include motor vehicle accidents,6,8,10,11 physical assault,9 falls from stairs, and a dhoti (traditional Indian male garment) being caught in an engine belt.12 The only reported case of IJBO after knee kick trauma was by Coskun et al. in 2007.7 Our case is only the second reported incident.

The proposed mechanism of a blow-out injury is the sudden transient rise in the intraluminal pressure of the hollow viscous because of compression force.12 In our case, the patient fell from a height of about 10 feet onto the knee of his friend, leading to trauma to the upper abdomen. External compression probably caused a sudden rise in the intraluminal pressure and eventually led to jejunal blow out. The patient initially felt pain, but it faded after some time. The initial pain was because of the trauma, but later the pain worsened because of spillage of the intestinal contents. Full blown peritonitis and septic shock developed over the week following the injury.

In all reported cases, the time of presentation was just after the trauma although in some cases
diagnosis was delayed for some time because of diagnostic uncertainty. A maximum in-hospital delay of 72 hours was reported by Kouritas in 2009 in a patient with thoracic trauma having occult jejunal perforation.\textsuperscript{10} In a community where there is no immediate access to medical services, patients may wait longer before reaching tertiary health care facilities. In our case, the trivial nature of the trauma complicated the picture even more. Presentation was 10 days after the trauma; however, there was only a minimal delay of 4 hours between presentation and surgical exploration.

A physical examination is generally not sensitive enough to make an accurate diagnosis,\textsuperscript{13} especially in cases where patients present before the development of peritonitis. In patients who do present with peritonitis, the symptoms may be confused with traumatic pancreatitis. Measurement of serum pancreatic enzymes and X-ray findings suggestive of intestinal perforation may be helpful in distinguishing between the two. However, an abdominal CT scan provides more accurate diagnosis.

The diagnostic accuracy of abdominal X-rays in identifying free air under the diaphragm is very low, and the chances of missing IJBO are very high.\textsuperscript{13} However, a delay in presentation allows sufficient time for the free air and fluid to accumulate in the peritoneal cavity. Moreover, bacteriological activity on the gastrointestinal contents also produces excessive air, which can lead to the formation of extraluminal air-fluid levels detectible through erect abdominal X-rays. In such cases, an X-ray of the abdomen in erect and supine positions can provide valuable information in the form of the identification of free air under the right hemidiaphragm, a ground glass appearance, and multiple intraluminal air-fluid levels. Nevertheless, these findings are not specific to IJBO because a similar picture may be seen in any kind of intestinal perforation presenting late, like peptic ulcer perforations, traumatic ileal perforations, or large gut perforations (caecal/colonic/rectal). Moreover, certain cases of extensive caecal dilatation, which may occur because of distal colonic obstruction,\textsuperscript{14} may have intraluminal air-fluid levels, which may be mistaken for extraluminal ones. Careful observation and the absence of free air under the diaphragm may help in distinguishing between the two. The role of the CT scan and laparoscopy in the evaluation of patients with blunt trauma is emerging and has replaced diagnostic peritoneal lavage (DPL).\textsuperscript{15} The CT scan has a sensitivity of 92% and a specificity of 94% in the detection of hollow viscous injuries.\textsuperscript{16} Laparoscopy has an additional benefit of being therapeutic in a certain percentage of cases;\textsuperscript{17} however, in patients who are haemodynamically unstable or present late with features suggestive of peritonitis, laparotomy will be required and peritoneal lavage will be necessary for the primary closure of the perforation.

The morbidity and mortality in small bowel perforation is lower than in colonic perforations. Delayed presentation, perforation with shock, and associated organ injuries are the factors which lead to higher morbidity and mortality in such cases.

**Conclusion**

IJBO is a very rare clinical entity. It may occur even after minimal abdominal trauma. In cases presenting with minimal abdominal signs, diagnosis is very difficult and a high index of suspicion is required where the mode of injury is suggestive of the possibility of IJBO. In such cases, radiological investigations like an abdominal CT scan may be helpful. Laparoscopy has an additional benefit, as an isolated perforation can be repaired by minimal
access surgery. If presentation is delayed, signs of perforation peritonitis and systemic signs of toxicity may be evident. In such cases, abdominal X-rays may show free air under the diaphragm or, rarely, extra-luminal air-fluid levels. Such patients should undergo exploratory laparotomy and surgical repair of the perforation. Early diagnosis with the help of radiological investigations like abdominal CT scans or laparoscopy is helpful in reducing the morbidity and mortality in cases of IJBO.

References

A hernia is defined as a protrusion of the small intestines or omentum through a defect in the abdominal wall. Hernias present as bulges in the groin area that can become more prominent when coughing, straining, or standing up. Although inguinal hernias are more common in males, they still can occur in females, most commonly in tandem with herniation of the omentum or small bowel. It is rare to find unusual contents in the hernia sac. A retrograde analysis of 1,950 cases of operable inguinal herniae showed that the vermiform appendix was present in 0.51% of the cases, ovaries and fallopian tubes in 2.9%, and urinary bladder in 0.36%.1 We report here on unusual contents within a hernia sac in an adult female who presented with symptoms and signs of an incarcerated left inguinal hernia. The left ovary contained a haemorrhagic cyst and, along with the left fallopian tube and broad ligament, these were found in the sac. She underwent a left ovarian cystectomy and the inguinal hernia was repaired with mesh.

Case Report

A married 31-year-old woman with two children who was known to have sickle cell disease, presented to the Accident and Emergency Department of Sultan Qaboos University Hospital, Oman, with a 5-day history of left-sided inguinal swelling associated with colicky abdominal pain and loss of appetite. She denied any history of constipation, nausea or vomiting. She was also known to have bronchial asthma, which was controlled with inhalers. Clinically, she was in distress with haemodynamically normal vital signs. Local examination revealed a 7 x 5 cm non-pulsatile, smooth-surfaced, warm, tender, irreducible swelling with a positive cough impulse. The rest of the systemic examination was within normal limits. Her routine blood workups were normal except for a leucocytosis of 13 x 10^9/L. A diagnosis of strangulated inguinal hernia was made and she was taken for emergency surgery after adequate resuscitation with intravenous fluids and...
antibiotics.

On exploration of the left inguinal canal, a thin sac containing a partially torted left ovarian cyst with a viable ovary and fallopian tube was found [Figures 1 and 2]. She underwent a left ovarian cystectomy and the inguinal hernia was repaired with Ethicon UltraPro mesh, (size 15 x 15 cm, Johnson & Johnson Medical Ltd., Ascot, UK). A histopathology study confirmed the finding of a haemorrhagic corpus luteum cyst. The patient had an uneventful recovery and was discharged home in a stable condition, with no recurrence seen on her recent follow-up appointment in the surgical clinic 6 months after surgery.

**Discussion**

The inguinal canal in the female is not well-demarcated as compared to the inguinal canal in males. Normally, different structures pass through it including the round ligament of the uterus, a vein, an artery from the uterus that forms a cruciate anastomosis with the labial arteries, and extra peritoneal fat.²

It is reported in literature that ovarian hernias are extremely rare in premenopausal women. On the contrary, most cases of gonadal hernias were reported in the paediatric age group in association with other genital tract anomalies.³ T. Okada et al. suggested a few hypotheses as to the mechanism by which this may occur.⁴ One of these hypotheses speculates that weakness of the broad ligaments or ovarian suspensory ligaments can contribute to ovarian herniation into the inguinal ring. This can be augmented by high intra-abdominal pressure as a result of carrying heavy things, or due to a chronic cough secondary to respiratory disease, as could be the case with our patient.

Although considered extremely rare, there have been case reports of different unusual contents found in inguinal hernia sacs, including parts of the genitourinary tract. McMillan reported a case of a rudimentary uterus in a 30-year-old female which had presented as a right groin lump for eight years.⁵ Despite the efforts made to diagnose the contents of inguinal hernias prior to surgery, most of them are made intraoperatively, as in our patient. Yao et al. suggested that in premenopausal women the morphological characteristics of the ovary in the hernia sac can be assessed through sonographic examinations, which provide information on ovarian function that cannot be obtained in younger females. These characteristics include eliciting a mass with multiple small sonolucent cysts indicating the ovary. A hyperechoic portion of the mass surrounded by an arterial flow can be observed on colour Doppler ultrasonography consistent with the presence of a corpus luteum. Furthermore, transabdominal sonographic scans of the pelvis may reveal the absence of one ovary in the lower pelvis on the same side as the inguinal hernia.⁶

Although ovarian cysts are not commonly encountered by surgeons, a high index of suspicion is required in order to avoid any delay in diagnosis and treatment. It was reported that about 4–37% of female inguinal hernias, which have been found intraoperatively, present with non-reducible
ovaries. Ovarian torsion and infarction have been encountered in 2–33% of these patients, which necessitates treating all cases, even when asymptomatic.7

Ovarian cysts can be dealt with effectively with the help of laparoscopy, particularly if the cyst is benign, with concomitant repair of inguinal hernia if the diagnosis is made preoperatively.8 This was not applicable in our patient as our preoperative diagnosis was a strangulated inguinal hernia.

Conclusion
In most cases, the contents of the hernia sac can be detected intraoperatively. Although considered to be a very rare entity, the possibility of ovarian hernia should be kept in mind in a female patient presenting with an irreducible swelling in the inguinal or femoral region in order to avoid serious complications. Whenever suspected, it must be treated as a surgical emergency.

References
Unusual Presentation of Oral Squamous Cell Carcinoma in a Young Woman

Diurianne CC França, Lira M Monti, Alvimar L de Castro, Ana MP Soubhia, Luiz ER Volpato, Sandra MHC Á de Aguiar, Marcelo C Goiato

CASE REPORT

Unusual Presentation of Oral Squamous Cell Carcinoma in a Young Woman

Diurianne CC França,1 Lira M Monti,2 Alvimar L de Castro,3 Ana MP Soubhia,4 Luiz ER Volpato,3 Sandra MHC Á de Aguiar,4 *Marcelo C Goiato4

Abstract:
Oral squamous cell carcinoma (OSCC) is the most common oral malignant neoplasm, mainly affecting individuals over 50 years old with a history of tobacco and alcohol use. The occurrence of this oral cancer in individuals under 45 years old is unusual and, when it does occur, shows a weaker relation to those risk factors and a more aggressive clinical course. Due to the paucity of reports in this population, it is difficult to prove its increasing trend. A case of oral squamous cell carcinoma in a 39-year-old woman with no history of tobacco or alcohol use is reported. Clinical and histopathological findings, aetiology, and treatment are discussed. The increasing trend of oral squamous cell carcinoma in young women without known risk factors highlights the need for clinicians to be aware of this rare occurrence.

Keywords: Carcinoma, Squamous cell; Mouth neoplasms; Risk factors; Case report; Brazil.

Throughout the last century, the number of cancer cases increased worldwide, now representing one of the most important public health problems in the world. The incidence of oral cancer has also increased.1 Oral squamous cell carcinoma (OSCC) represents between 90% and 95% of all malignant neoplasms of the oral cavity. Lesions are located mainly on the tongue, especially on the lateral posterior border.2 Historically, scientific literature has demonstrated a preferential incidence of oral cancers in men aged 50 to 70 years.2,5 However, recent epidemiological studies have shown an increase in the development of OSCC in patients under 45 years old.6,9 In those cases, tumour behaviour is different and patients have a poor prognosis in comparison to cancer in older adults.10

The modification of social and cultural habits, specifically those concerning male and female behaviours, could be related to the increase in the occurrence in women.1,11,12 However, the absence of traditional risk factors such as alcoholism and excessive tobacco use6,7 in young patients has suggested that in these cases cancer may be
a different disease from that occurring in older patients, and may have a different aetiology and clinical progress.\textsuperscript{13–15}

In this article, we report the case of OSCC in a woman with no history of tobacco or alcohol use, and discuss the clinical and histopathological findings, aetiology and treatment.

Case Report

A 39-year-old female patient with no history of alcoholism, excessive tobacco use, or any other harmful habit, sought treatment for the complaint of an ulcerated lesion with one month’s evolution in the buccal mucosa. The lesion was defined by the patient as a common aphthous ulcer. The patient revealed a family history of cancer, as her grandmother had died of stomach cancer.

Clinically, facial asymmetry with tumefaction at the right side was observed [Figure 1]. Intra-orally, there was an ulcerated lesion 5 cm in diameter, with irregular borders, and a necrotic bed located at the right buccal mucosa [Figure 2]. Whitish areas could be observed in the periphery of the ulceration. The radiographic examination did not reveal any signs of bone destruction, and the proposed clinical diagnosis was a traumatic ulcer.

An incisional biopsy was performed. Areas of great inflammatory infiltrate were identified as well as hornish pearls, intact stratified pavmented epithelium, islets of neoplastic epithelium, polymorphism, and hyperchromatism, thus establishing the diagnosis as OSCC [Figure 3]. The tumour-node-metastasis (TNM) staging system revealed was stage III disease (T3N0M0) based on the mouth cancer TNM classification criteria of the American Joint Committee for Cancer Staging (UICC/AJC).

The patient was referred to an oncological centre for treatment, which included surgery for resection of the oral mucosa involving the upper alveolar ridge, labial commissure, and mandibular retromolar area, and radiotherapy (5040 cGy). Currently, the patient is in complete remission, and follow-up treatment includes speech therapy and nutritional counselling.

Discussion

OSCC occurs less frequently in young individuals (<40 years). Those cases represent 3 to 6% of all OSCCs.\textsuperscript{3,4,7} In up to 72% of these younger patients, one or more behavioural risk factors are present. Also, men are affected twice as often as women.\textsuperscript{16}

Of the many different factors associated with an increased risk for OSCC, tobacco and alcohol seem to be the most studied. Individuals who smoke more than 20 cigarettes a day and consume more than 100 g of alcohol a day are at increased risk of oral epithelial dysplasia, but ex-smokers of 10 or more years seem to have no greater risk than non-smokers.\textsuperscript{16}

Few reports have shown distinct molecular differences between younger and older patients with OSCC, as well as between non-smoking and smoking patients, supporting the hypothesis that different subgroups of OSCC exist, especially with respect to exposure to tobacco carcinogens.\textsuperscript{7}
It is hypothesised that a subgroup of individuals, characterised by the development of the disease at early ages and by shorter exposure time to behavioural risk factors, develops a histologically similar, but genetically different OSCC, as compared to their older counterparts. This may be due to an increased susceptibility to the development of oral cancer as a result of a lower expression of single nucleotide polymorphisms of the GSTP1 gene. This encodes an enzyme that functions in xenobiotic metabolism of polycyclic aromatic hydrocarbons, which is involved in the metabolism of carcinogens and/or DNA repair, as seen in other tumour types.7

Clinical manifestations of OSCC in younger patients have no features to distinguish them from that of older patients; nevertheless, many clinicians tend not to include OSCC as a differential diagnosis in young patients, simply because such disease does not often present in that age range.2

The reported case presents different characteristics from the OSCC usually reported in epidemiological studies; the patient was young and without a history of alcoholism or excessive tobacco use. In this case, in consideration of the family’s health history, the genetic hypothesis must be reinforced in the lesion aetiology. This is consistent with the observation of other workers who report OSCC without a history of alcoholism or excessive tobacco use.3,14,17

Alcoholism or excessive tobacco use have been reported in only a small number of young patients, and even in cases where a correlation is found, the exposure to carcinogens was not sufficient for the development of a malignant lesion.3,18 Moreover, many people are exposed to such risk factors and only a small percentage develops the disease, which determines the necessity of searching for other risk factors such as immunological or nutritional deficiencies, genetic factors, and microbiological agents in etiogenesis. Among these factors, human papillomavirus and Epstein-Barr virus have already been suggested as aetiological factors.1,12

In summary, the factors that should be investigated in order to explain the aetiology of OSCC in young patients, include genetic predisposition, previous viral infections, nutritional patterns, immunodeficiency, occupational exposure to carcinogens, socioeconomic conditions, and oral hygiene.2 There is some agreement regarding the poor prognosis and short survival rates in younger patients who develop OSCC in the absence of the usual risk factors,3 although some studies were based on small numbers of patients.4,15

**Conclusion**

We described the case of a 39-year-old lady who was diagnosed to have OSCC of the buccal mucosa.2,16 There were no known risk factors. OSCC in this age is rare, but should always be considered in the differential diagnosis of non-healing buccal ulcers. The association a young female patient without exposure to the most common risk factors, and more aggressive tumoural behavior in an unusual area, suggest that OSCC, when occurring in non-smokers, represents a different clinical
and molecular disease. Further studies would be necessary to identify other risk factors involved in tumoural development in order to improve prevention programmes and early detection.

References


The contents of inguinal hernia sacs differ from case to case. Various structures contained therein have been described, but the presence of the appendix in an inguinal hernia sac is rare. This anomaly was first described by Claudius Amyand in an 11-year-old boy who underwent a successful appendectomy in 1735. The incidence of appendicitis within an inguinal hernia is estimated at 0.07–0.13 %. The eponym Amyand’s hernia was first coined by Creese in 1953, then by Hiatt and Hiatt in 1988, followed by Hutchinson in 1993. We report four cases of Amyand’s hernia which were treated at Sultan Qaboos University Hospital, Oman. All patients underwent appendectomy. In three cases, the inguinal hernia were repaired with Vipro mesh while, in the remaining case, a darning repair was done with Prolene sutures.

**Keywords:** Inguinal hernia; Appendix in hernia; Acute appendicitis; Case report; Oman.
swelling extending up to the base of the scrotum. The lump was tense, tender, and irreducible. Both testes were palpable in the scrotum. After adequate resuscitation he was taken to surgery under general anaesthesia.

The left inguinal canal was explored, and a strangulated irreducible indirect inguinal hernia was found, with constriction at the external ring. About 1.2 litres of an amber-coloured fluid was aspirated upon opening the sac, and the gangrenous caecum and appendix were removed. The small bowel loops were dusky initially, but became pink upon release of the constriction. The contents of the sac were pushed inside and a lower midline laparotomy was performed. A gangrenous floppy mobile caecum was seen, along with a gangrenous appendix which had herniated through the deep ring on the left side. There was no situs inversus or malrotation of the gut. The rest of the viscera were normal. A limited right hemicolectomy was done with ileocolic anastomosis. Before closing the abdomen, the hernia was repaired by darning with size 0 Prolene (Ethicon, Inc., Manlo Park, California, USA). The patient was treated with broad spectrum antibiotics and had an uneventful recovery. The histopathology was consistent with a gangrenous caecum and appendix. After one year, the patient was well with no recurrence of the hernia.

Case Two

A 19-year-old male was admitted for right inguinal hernia repair. He had had the hernia for six months. It was increasing in size, especially during walking, but was reducible upon lying down. Examination showed swelling in the right inguinal region, which was non-tender, partially reducible, and had a positive cough impulse. The patient underwent inguinal hernia repair under general anaesthesia. Per-operatively, he was found to have an indirect sac containing a congested appendix with palpable fecolith. An appendectomy was performed and repair of the hernia was accomplished with Vipro mesh (Ethicon, Inc., Manlo Park, California, USA). The patient had an unremarkable recovery and was discharged three days after the surgery. He was seen for follow-up after one month; the incision site was uninfected. The histopathology result showed a
congested appendix with lymphoid hyperplasia.

**Case Three**

A 75-year-old male presented with a 2-month history of swelling in the right inguinal region, which had increased recently causing discomfort but no significant pain. It was reducible with incomplete swelling, but the patient had a positive cough impulse. On exploration of the inguinal canal, the appendix was discovered to be adherent to an indirect hernia sac. The appendix was normal looking, but was removed after dealing with the adhesions. The histopathology revealed an inflamed appendix. The posterior wall was repaired with Vipro mesh (Ethicon, Inc., Manlo Park, California, USA) and the patient was discharged two days after surgery. He was seen for follow-up one month after surgery and there was no infection at the surgical site. On his last visit to the surgical clinic, two years after surgery, no recurrence was found.

**Case Four**

A 26-year-old male was admitted for an elective repair of a right-sided inguinal hernia. He had had reducible swelling for the previous two years. The hernia had recently become partially irreducible, but the patient was without pain or any other symptoms other than a positive cough impulse. Per-operatively, it was noted that he had an indirect inguinal hernia, and a caecum and appendix which were not inflamed on gross appearance. An appendectomy was performed along with repair of the hernia with Vipro mesh (Ethicon, Inc., Manlo Park, California, USA). He recovered without any complications. Histopathology of the appendix was consistent with lymphoid hyperplasia without any inflammation. He was doing well three years after surgery.

**Discussion**

A hernia is the protrusion of the viscus or a part of the viscus through the wall of its containing cavity. By far the most commonly encountered hernia is in the inguinal region which also normally contains bowels, or omentum. Among the unusual contents are the bladder, Meckle’s diverticulum (known as Littre’s hernia), or a portion of the circumference of the intestine (called Richter’s hernia), but Amyand’s hernia is relatively unknown despite being first reported in 1735 by Claudius Amyand.1

The term Amyand’s hernia is used to refer to a hernial sac containing an inflamed or non-inflamed appendix in an irreducible inguinal hernia.7 Losanoff and Basson suggested a distinct classification to improve the management of Amyand’s hernias.8

The incidence of a normal appendix being found inside an inguinal hernia sac is about 1%; however, only 0.1% of these cases have appendicitis.9 Solecki et al. observed that acute appendicitis was found in 0.62% of all groin hernia sacs.10 In most of the patients who present with a right-sided Amyand’s hernia, its location can be explained by the normal anatomical position of the appendix; also, right-sided inguinal hernias are more common. In this study, three patients had right-sided hernias. However, left-sided Amyand’s hernias have also been described in the literature and may be associated with situs inversus, malrotation of the gut, or mobile caecum, as was found in one of our cases.6,12

The pathophysiology of Amyand’s hernia is unknown. Weber et al. proposed that due to herniation the appendix can become more

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**Table: Classification of Amyand’s hernias**8

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
<th>Surgical management</th>
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</thead>
<tbody>
<tr>
<td>Type I</td>
<td>Normal appendix in inguinal hernia</td>
<td>Hernia reduction, mesh repair; appendectomy in young patients</td>
</tr>
<tr>
<td>Type II</td>
<td>Acute appendicitis within an inguinal hernia and no abdominal sepsis</td>
<td>Appendectomy through hernia; primary repair of hernia; no mesh</td>
</tr>
<tr>
<td>Type III</td>
<td>Acute appendicitis within an inguinal hernia or the abdominal wall, or peritoneal sepsis</td>
<td>Laparotomy; appendectomy; primary repair of hernia; no mesh</td>
</tr>
<tr>
<td>Type IV</td>
<td>Acute appendicitis within an inguinal hernia with related or unrelated abdominal pathology</td>
<td>Manage as hernias type I–III; investigate or treat second pathology as appropriate</td>
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</table>
vulnerable to micro-trauma, causing adherence to the hernia sac due to fibrosis. This hypothesis that inflammatory swelling may lead to incarceration, subsequent impaired blood supply, and bacterial overgrowth was supported by Abu Dalu, Barut, and House. Muscle contractions and changes in abdominal pressure can cause compression of the appendix, resulting in reduced blood supply and secondary inflammation.

Diagnosing Amyand’s hernia pre-operatively is not straightforward. In the majority of cases, it is diagnosed when the hernia sac is opened, as most patients undergo emergency surgery. Although a preoperative computed tomography (CT) scan of the abdomen can be helpful in diagnosing the condition, it is not routinely employed in such cases. If the diagnosis is established by CT, it is possible to treat Amyand’s hernia laparoscopically.

The recommended treatment is appendectomy with primary hernia repair. Use of synthetic mesh is avoided in the repair of contaminated abdominal defects because prosthetic material can increase the inflammatory response and result in wound infection and a rare but possible complication of appendiceal stump fistula. Preigo et al. carried out appendectomies in six patients, using mesh in three. One patient developed a wound infection after being treated with mesh. Bailey reported a wound infection rate of 3% in hospital that went up to 9% in community surveillance. However, Saggar et al. reported endoscopic total extraperitoneal repair with mesh in a right-sided incarcerated inguinal hernia without any complications.

We performed appendectomies in all of our cases and repaired the hernia with mesh in three of our patients. In Case 1, we decided not to use mesh due to the presence of a gangrenous appendix. This guarded the hernia from a possible future extension of inflammation into the mesh. However, we did repair the hernia with mesh in cases 2 to 4 as the appendices were mildly inflamed with no purulent fluid in the hernial sac. The follow-up period in our patients ranged from one month to three years with no surgical site infection seen during the immediate post-operative period. No recurrence of the hernias was found.

**Conclusion**

Amyand’s hernia is a rare clinical entity that is difficult to diagnose pre-operatively. The presence of an inflamed or gangrenous appendix increases the rate of complication, particularly increasing the rate of wound infection. Diagnosis is usually made at the time of surgery, which is usually indicated in all incarcerated hernias. Consequently, our recommendation is that the decision to perform an appendectomy and/or to use mesh to repair hernias should always be individualised.

**References**

Amyand’s Hernia
Study of four cases and literature review

METHEMOGLOBINEMIA IS AN infrequent haematological disorder that can result from congenital and acquired conditions. The congenital form is rare and not always compatible with life, but acquired methemoglobinemia is more common and can result from a wide variety of environmental agents, including prescribed and recreational drugs. Oxygen therapy and intravenous methylene blue is usually the first line treatment for this disorder. A high level of suspicion is necessary for the accurate and timely diagnosis of this condition, as any delay can be catastrophic.

Case One

A 39-year-old male with no significant past medical history presented to the emergency department after collapsing following recreational ingestion of alkyl nitrates (‘poppers’). He denied using any other recreational, prescribed, or over-the-counter drugs. Upon presentation, the patient was fully awake and oriented, with a Glasgow Coma Score (GCS) of 15/15, and no significant abnormal findings on initial clinical examination. The electrocardiogram (ECG), chest radiograph, and initial blood investigations were within the normal stated local limits. Pulse oximetry revealed oxygen saturations of 85–88% whilst breathing room air.

Arterial blood gas (ABG) analyses and oxygen saturations as measured on pulse oximetry are shown in Table 1. A diagnosis of acquired methemoglobinemia was made and, as such, definitive treatment with high flow oxygen (15 litres delivered via a non-rebreathing mask) and intravenous methylene blue (1.5 mg/kg infused over 10 minutes) was initiated. The measured ABG (including methaemoglobin [MetHb] levels) returned to within normal limits within 24 hours of his admission, as shown in Table 1.
Acquired Methemoglobinaemia

The patient was discharged after an uneventful 48-hour inpatient stay, having received counselling regarding the potential dangers associated with the misuse of poppers.

Case Two

A 40-year-old male with a significant smoking history was found collapsed after ingesting two beers and a bottle of poppers within a period of 30 minutes. The patient voluntarily provided a full glass bottle similar to the one ingested [Figure 1].

On arrival in the emergency department the patient was fully orientated, with a GCS of 15/15. On clinical examination he was unkempt with tar-stained fingers. The patient was also noted to be centrally cyanosed with a mild bilateral expiratory wheeze. The rest of the initial clinical examination was largely unremarkable. An ECG revealed a sinus tachycardia with left axis deviation. ABG analyses and oxygen saturations as measured on pulse oximetry are shown in Table 2.

Acquired methemoglobinaemia with possible previously unidentified chronic obstructive pulmonary disease was diagnosed; therefore, the patient was started on monitored high flow oxygen therapy with serial clinical assessments and ABGs, as well as intravenous methylene blue. The patient was discharged after education about the potential effects of abusing poppers, smoking cessation advice, and inhaled bronchodilator therapy for his probable chronic obstructive pulmonary disease. He was also given follow-up appointments with the chest clinic for further evaluation of his chest condition, but he did not attend.

Discussion

Methemoglobinaemia is a disorder in which the haemoglobin (Hb) molecule is altered to prevent efficient carriage of oxygen, essentially shifting the oxygen dissociation curve to the left, leading to a functional anaemia. A variety of aetiologies including genetic, dietary, idiopathic, and toxicological have been implicated. Acquired methemoglobinaemia is much more common than the hereditary form, occurring when an exogenous substance oxidises Hb to methaemoglobin (MetHb) at rates of 100 to 1000 times greater than it can be reduced back to its original form [Figure 2]. Congenital methemoglobinaemia can occur from a cytochrome b5 reductase deficiency or from a structural Hb defect, collectively called HbM. There

<table>
<thead>
<tr>
<th>Table 1: Case 1 arterial blood gas (ABG) results and measured oxygen saturation (SaO2) on pulse oximetry</th>
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<tbody>
<tr>
<td><strong>Inspired oxygen (FiO2)</strong></td>
</tr>
<tr>
<td>----------------------------</td>
</tr>
<tr>
<td><strong>SaO2</strong></td>
</tr>
<tr>
<td><strong>PaO2</strong></td>
</tr>
<tr>
<td><strong>PaCO2</strong></td>
</tr>
<tr>
<td><strong>MetHb %</strong></td>
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</table>

Legend: FiO2 = fraction of inspired oxygen; SaO2 = oxygen saturation; PaO2 = partial pressure of oxygen in blood; PaCO2 = partial pressure of carbon dioxide in blood; MetHb = methaemoglobin; kPa = kilopascal.

Figure 1: Bottle of alkyl nitrite provided by Patient 2
are two types of congenital methaemoglobinaemia. In type 1, the enzyme deficiency is confined to the red blood cells, whereas in type 2 a range of cells, including brain cells, is affected. Type 2 usually results in mental retardation, neurological abnormalities, or death in childhood. Lifelong use of agents having the same effect as the deficient reducing enzyme, such as ascorbic acid (vitamin C) and/or riboflavin (vitamin B2) can be used to try to alleviate some of the clinical features of the condition, especially in type 1. HbM results from a single amino acid substitution in either alpha or beta polypeptide chains at the region where the iron-containing heme portion is attached. This results in a failure to convert MetHb to Hb.3

Normally, there is a continuous conversion of Hb to MetHb, and vice versa. The reduction of MetHb to Hb happens through two different pathways. The nicotinamide dinucleotide (NADH)-dependent cytochrome b5-methaemoglobin reductase pathways account for 99% of MetHb reduction to Hb. The other mechanism depends on utilising nicotinamide-adenine dinucleotide phosphate hydrogenase (NADPH) generated by glucose-6-phosphate dehydrogenase (G6PD) in the hexose monophosphate pathway. This mechanism is physiologically inactive and needs extrinsic agents, like methylene blue, to activate it. Whereas the former mechanism is the main physiologically active reducing mechanism, the later pathways are highly important when the physiologically active mechanism is overwhelmed and the therapeutic correction of MetHb is attempted via methylene blue.3

Poppers are potent oxidisers of oxyhaemoglobin (converting Fe²⁺ to Fe³⁺) resulting in the formation of MetHb, and are volatile liquids that are sometimes abused by both sexes for euphorigenic rushes and altered states of consciousness. The name ‘poppers’ may have been derived from the sound caused by breaking open the glass vials which were originally used to store the volatile contents.4 Methemoglobinaemia has been reported to develop after the ingestion of as little as 10 ml of alkyl nitrite.5 Factors that may predispose to pharmacologically-induced methemoglobinaemia include the use of large quantities of the offending agent, any discontinuation of the body’s normal mucosal barriers, and the concomitant use of other drugs known to cause methaemoglobinaemia, such as acetaminophen (paracetamol), primaquine, or cocaine.6 In addition, dapsone has been implicated in almost 50% of cases of acquired methaemoglobinaemia, which is clinically important as, due to its relatively long half-life, cimetidine may be required to try to block its

Table 2: Case 2 arterial blood gas (ABG) results and measured oxygen saturation (SaO₂) (on pulse oximetry)

<table>
<thead>
<tr>
<th></th>
<th>Normal range</th>
<th>Admission</th>
<th>24 hours after admission</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inspired oxygen (FiO₂)</strong></td>
<td>Room air (0.21)</td>
<td>Non-rebreath reservoir mask at 15L/min O₂ (~ 0.90)²</td>
<td>Room air (0.21)</td>
</tr>
<tr>
<td><strong>SaO₂</strong></td>
<td>&gt;96%</td>
<td>90%</td>
<td>96%</td>
</tr>
<tr>
<td><strong>PaO₂</strong></td>
<td>10–13 kPa</td>
<td>8.3 kPa</td>
<td>8.3 kPa</td>
</tr>
<tr>
<td><strong>PaCO₂</strong></td>
<td>5.4–6.8 kPa</td>
<td>6.2 kPa</td>
<td>6.1 kPa</td>
</tr>
<tr>
<td><strong>MetHb %</strong></td>
<td>&lt;1% (non-smokers)</td>
<td>46.0%</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

Legend: FiO₂ = fraction of inspired oxygen; SaO₂ = oxygen saturation; PaO₂ = partial pressure of oxygen in blood; PaCO₂ = partial pressure of carbon dioxide in blood; MetHb = methaemoglobin; kPa = kilopascal.

Figure 2: The role of methylene blue in the treatment of methaemoglobinemia

Legend: G6P = glucose 6 phosphate; G-6-PD = glucose-6-phosphate dehydrogenase; RSP = ribose-5-phosphate; NADP = nicotine adenine dinucleotide phosphate; NADPH = nicotine adenine dinucleotide phosphate hydrogenase; MetHb = methaemoglobin; Hb = haemoglobin.
metabolism via hepatic microsomal cytochrome P450 (CYP450). Topical local anaesthetic agents (e.g. lidocaine or benozocaine) for procedures such as bronchoscopy, laryngoscopy, or upper gastroduodenoscopy can also result in acquired methaemoglobinaemia. Another risk factor for developing pharmacologically-induced methaemoglobinaemia is the presence of concomitant illnesses, including cardiac and respiratory diseases.

This condition should be suspected if cyanosis develops after suspected exposure to potent oxidizing agents, or if chocolate brown arterial blood does not turn red on exposure to air. Some of the more common non-specific clinical features are listed in Table 3. However, clinical presentation may vary greatly and definitive treatment with methylene blue might not always be needed depending on the clinical condition.

Pulse oximetry is a useful tool to diagnose suspected methaemoglobinaemia. It basically works by emitting lights at two different wavelengths (660 nm in the red spectrum wavelength and 940 nm in the infrared spectrum wavelength). These wavelengths are absorbed differently by deoxyhaemoglobin and oxyhaemoglobin (i.e. deoxyhaemoglobin absorbs more light at 660 nm wavelengths and oxyhaemoglobin absorbs more light at 940 nm wavelengths). By calculating the differences, the microprocessor in the pulse oximeter can measure the SaO2 (sometimes referred as SpO2 when measured by a pulse oximeter). Whereas MetHb absorbs more light than either oxyhaemoglobin and deoxyhaemoglobin at 940 nm wavelength, its absorption is similar to that of deoxyhaemoglobin at 660 nm wavelengths resulting in falsely low SaO2 due to an incorrectly high deoxyhaemoglobin perception by the pulse oximeter. However, newer pulse oximeters are able to omit light at 8 different wavelengths making it possible to measure MetHb and carboxyhaemoglobin as well.

The diagnosis of methemoglobinaemia can be confirmed with an ABG sample that demonstrates a discrepancy between arterial oxyhaemoglobin saturation (SaO2) and measured arterial oxygen partial pressure (PaO2). A high saturation gap should also lead to the suspicion of methaemoglobinaemia. The gap is defined as the difference between oxygen saturation measured by the pulse oximeter and that calculated by ABG. This gap is usually >5 in cases of methaemoglobinaemia.

Methylene blue can be an effective treatment for acquired methemoglobinaemia and should be administered at a dose of 1–2 mg/kg intravenously over 3–10 minutes. An obvious clinical improvement should be evident within one hour, but if cyanosis persists, a second dose may be considered. Higher doses of methylene blue (>7 mg/kg) may cause haemolysis and persistent cyanosis, as the agent can paradoxically oxidise haemoglobin to MetHb, as opposed to acting as a reducing agent at lower doses. Relapsing methemoglobinaemia has also been described in the literature with a delayed, biphasic rise in the level of MetHb. This may be due to a secondary paradoxical cyclical formation of MetHb by the offending agent (e.g. dapsone or methylene blue). CYP450 inhibitors (e.g. cimetidine) and exchange transfusion might be needed to treat these patients. Also, individuals with G6PD deficiency may not produce sufficient NADPH to reduce methylene blue to leucomethylene blue, potentially rendering the therapy ineffective. Furthermore, methylene blue might induce haemolysis in G6PD-deficient patients. Alternative treatments with cimetidine, ascorbic acid, and possibly exchange transfusions, should be considered in patients with a G6PD deficiency. N-acetylcysteine is also under study as a possible treatment for this category of patients.

**Conclusion**

We report a fatal medical condition which may result from the abuse of a widely-available recreational drug. Physicians in acute medical specialties should have a raised clinical suspicion

<table>
<thead>
<tr>
<th>MetHb concentration %</th>
<th>Possible clinical features may include</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>Often asymptomatic</td>
</tr>
<tr>
<td>10–20</td>
<td>Cyanosis, skin discoloration</td>
</tr>
<tr>
<td>20–50</td>
<td>Anxiety, light-headedness, headaches, tachycardia</td>
</tr>
<tr>
<td>30–50</td>
<td>Fatigue, confusion, dizziness, tachypnoea</td>
</tr>
<tr>
<td>50–70</td>
<td>Coma, seizures, acidosis, arrhythmias</td>
</tr>
<tr>
<td>&gt;70</td>
<td>Death</td>
</tr>
</tbody>
</table>

Table 3: Common clinical features associated with approximate MetHb concentration
for this condition when there is a possible history of drug misuse and a significant discrepancy between the clinical picture and measured SaO₂ and PaO₂ levels. This raised level of awareness can ensure acquired methaemoglobinemia’s accurate diagnosis and timely treatment. Both of our patients were discharged safely after timely diagnosis and management of a potentially life-threatening condition.

ACKNOWLEDGMENTS

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References

A 45-year-old woman presented with refractory pulmonary oedema secondary to a massive thrombosis of a St. Jude mechanical mitral prosthetic valve. She was noncompliant with warfarin and had suffered embolic stroke 3 years earlier, from which she had recovered. She was in sinus rhythm with absent valve clicks on auscultation. A transthoracic echocardiogram revealed a high transmitral peak gradient of 34 mmHg and a mean gradient of 27 mmHg with an ejection fraction of 55% [Figure 1A]. The international normalised ratio (INR) was 1.29. An urgent transesophageal echocardiogram (TEE) demonstrated a large (6 cm²) left atrial thrombus attached to the mechanical valve at the discs which were stuck in a closed position [Figures 1B and 1C].

The patient was advised to have emergency surgery, but she and the family refused. In spite of explaining the risks involved in thrombolysing a large clot, the patient and the family preferred thrombolytic therapy. As a life-saving measure, the patient was thrombolysed with 10 units of reteplase intravenously over 2 minutes with a repeat dose of 10 units administered 30 minutes later. After an hour of thrombolysis a repeat TEE showed complete disappearance of the thrombus from the left atrium with one of the discs stuck in closed position [Figures 2 A and B]. The peak transmitral gradient was 7 mmHg and the mean gradient was 4 mmHg [Figure 2C]. Immediately, the patient started
to complain of severe pain in the left leg with cold periphery and absent femoral pulse on both sides. An urgent computed tomography angiogram of the abdomen, pelvis and legs demonstrated complete occlusion of left common iliac artery and right common femoral artery with reformation of distal arteries [Figures 3A, B and C]. An emergency open bilateral ilio-femoral embolectomy was performed and a large thrombus removed from the left common iliac artery [Figure 4 A and B]. Unfortunately, the patient developed refractory sepsis with acute renal shut down and died after 10 days of admission.

The incidence of left-sided prosthetic valve thrombosis (PVT) ranges from 0.5% to 0.8% per patient-year.1,2 The mortality of obstructive PVT is about 10% irrespective of the treatment strategy.1 The American College of Cardiology/American Heart Association (ACC/AHA) and American College of Chest Physicians guidelines recommend fibrinolytic therapy as first-line treatment for patients in good functional class with low thrombus burden (< 0.8 cm²) and in all other patients if they are considered to be at high risk for surgery.3,4 Emergency surgery is reasonable for patients with a thrombosed left-sided prosthetic valve and New York Heart Association (NYHA) functional class III–IV symptoms or a large clot burden (> 0.8cm²).3,4 Furthermore, in the following groups of patients...
surgery is advised, namely: 1) patients with large left atrial thrombus; 2) patients with any active bleeding or a history of intracranial bleeding; 3) patients with evidence of ischaemic stroke from 4 hours to six weeks, and 4) post-valve replacement within 4 days. The major complication of thrombolytic treatment for PVT is the risk of embolisation which occurs in 12–15% of the cases. A registry study demonstrated that thrombus size on TEE and a past history of stroke were independent predictors of complications as seen in this patient. Left atrial thrombi are also known to embolise at the time of, or shortly after a change in atrial rhythm. In this case, there was not only obstructive PVT, but it was associated with a large left atrial thrombus and hence surgery was the initial choice of treatment. However, the patient refused surgery and was thrombolysed with catastrophic embolism.

References

Sir,

The recent conclusion of SATURN (Study of Coronary Atheroma by InTravascular Ultrasound: Effect of Rosuvastatin versus Atorvastatin) study, demonstrated that maximal suggested doses of both atorvastatin and rosuvastatin ameliorate atherosclerosis to a similar extent by facilitating the regression of percent atheroma volume. Both statins, however, caused renal proteinuria, albeit to different extents. The published results of the study ephemerally state that “proteinuria was commoner in the rosuvastatin group than in the atorvastatin group (3.8% versus 1.7%)”. Further, the treatment group pertaining to atorvastatin had higher number of diabetics compared to the group on rosuvastatin (16.8% versus 13.8%). Diabetes augments kidney failure, accounting for nearly 44% of new cases in the United States, therefore it is plausible the atorvastatin treatment group had more patients with renal dysfunction than the rosuvastatin treatment group whereby the actual reported percentage of patients with proteinuria on rosuvastatin might not reflect the true value.

The median age of the participants in SATURN-trial is ~57 years. An individual of 57 years has an average glomerular filtration rate (GFR) of 93 ml/min/1.73m² versus 116 ml/min/1.73m² observed in individuals 20–29 years of age, indicating a decline in renal function with advancement with age. The intriguing issue of pivotal importance remaining unanswered is “Which statin should preferably be administered in patients who are elderly with declining renal function/chronic kidney disease (CKD) patients/patients with diabetic proteinuria?”

Currently, with contradicting results from several trials, a conclusive answer to the above is unavailable. As a case in point, atorvastatin exhibited reno-protective effects in the Treating to New Targets (TNT) study, but decreased estimated (e)-GFR in PLANET-I and CARDS trials. Similarly, rosuvastatin exhibited reno-protective effects in mouse-model experiments, but in PLANET-I it exhibited reno-deleterious effects as it significantly decreased e-GFR. The results of the SHARP trial show promise where simvastin plus
ezetimibe could be prescribed for patients with renal dysfunction, without plausible detrimental effects on renal health, although the trial lacked a longer follow-up period.\(^8\) Future head-to-head trials with different statins or a statins plus non-statin-cholesterol lowering drug combination, conducted in a patient population with CKD and with a suitable follow up period, are essential to answer the question posed above. In the meantime, clinicians will have to choose the statin appropriate to the need of the patient.

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Reference

Sir,

Recently, during a routine histopathological examination, an excisional biopsy of a squamous cell carcinoma, on the lateral border of the tongue of a 70-year-old male patient, was evaluated and revealed a remarkable feature. In a haematoxylin and eosin (H&E) stained slide, numerous well defined polygonal isomorphous tiny structures, the majority of them stained with eosin and a few unstained, filled a lumen-like structure formed by the folding of the thin stratified squamous epithelium [Figure 1a]. My fellow postgraduates suspected them to be some sort of desquamated epithelial cells, ghost cells, cross-sections of muscle fibres, keratin flakes, red blood corpuscles or inclusion dust, glass or metal particles. Moreover, in another field, a few elongated well defined semi-transparent structures, resembling candidal hyphae were seen interspersed with the numerous above mentioned structures [Figure 1b]. Since candidal hyphae hardly persist in formalin fixed tissue and can easily be differentiated by its pseudomycelium forms, we excluded this possibility.

An artefact (Latin 'ars'- art + 'factum'- made) in histology means any non-natural feature or structure accidentally introduced into something being observed or studied.1 Suture material is an occasional inclusion in histological specimens. It may consist of isolated fragments or complete fibre-bundles cut in transverse, oblique or longitudinal planes. Detail of the fibre structure can sometimes be seen upon careful examination of H&E stained sections. Silk sutures exhibit strong birefringence under polarised light and can be useful in their identification.2,3 Our suspicion in this case was confirmed when we observed the same sections under a polarising microscope. The sections of mysterious foreign material exhibited a strong birefringence under a polarised light [Figure 2]. Hence we concluded that the foreign material was polyfilament silk suture material (cross-sections and longitudinal sections).

Other artefacts with structures almost similar to suture filament include cellulose fibre and hair. Cellulose fibres arising from cotton gauze can be encountered as a contaminant during specimen collection and processing. It is recognised by the characteristic appearance of plant cells with their strongly staining cell walls and square shape. Very rarely a hair can also contaminate the tissue during processing; it can be

Figures 1A and 1B: Cross-sections (A) and longitudinal sections (B) of the polyfilament silk suture material when viewed under a bright field microscope (haematoxylin and eosin stain, x 20)
clearly differentiated by its characteristic tubular structure and black/brown colour. Moreover, in contrast to polyfilament sutures, and in the case of, too many cross-sections, hair will not be seen in a single section.2,3

The purpose of this letter is to call the attention to this artefact, which may be found during a histopathology routine, and needs to be kept in mind for an accurate diagnosis.

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References

Body Image and Self-Esteem Among Female Nursing Students in Three Different Arab Countries

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Current Western culture promotes standards of beauty and success which focus on physical attractiveness. These standards can create feelings of inadequacy and body dissatisfaction. Traditionally, women have responded most strongly to cultural messages of bodily attractiveness, thereby experiencing greater body dissatisfaction than men. Failure to achieve the ideal has been shown to lead to decreased self-esteem which compounds body dissatisfaction and body image disturbance. This study aimed to investigate the level of body image and self-esteem among three community-based samples from Riyadh, Saudi Arabia; Hadhramout, Yemen, and Assiut, Egypt. 300 students were recruited, 100 per country. The study was carried out in three different faculties of nursing: Riyadh Female Health Science College in Saudi Arabia, Hadhramout University of Science and Technology in Yemen, and at Assiut University in Egypt. Tools for data collection included the body image scale developed by El-Desouki. This scale consists of 20 statements about positive and negative sensations of body image. Also used was the Rosenberg self-esteem scale which consists of 10 statements about positive and negative self-esteem. Finally, an interview questionnaire, developed by the investigators, included information about students’ ages, residence, marital condition, economic condition, parents’ education level, number of brothers and sisters, and their sibling order. Results of this study revealed that 86% of students in Al-Riyadh, 84% from Assiut, and 73% from Hadhramout had positive self-images. The majority of the subjects had high self-esteem (78% in Al-Riyadh, 96% from Assiut and 84% from Hadhramout). It also found that 79.8% of the subjects with a positive body image had high self-esteem compared to only 20.2% of subjects with a negative body image had high self-esteem. In conclusion, a high level of self-esteem positively correlated with body image. Age, parents’ level of education, marital status, and number of brothers and sisters significantly correlated to body image and self-esteem. This study recommended that the importance of developing a positive body image and healthy diet habits is crucial.

Nurses’ Orientation Towards Lifelong Learning: A case study of Uganda’s national hospital

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The quality of nursing care in developing countries is poor and improvements via continuing education programmes are underway. Nurses’ orientation towards lifelong learning (NOLLL) has not been explored despite its potential effect on the success of such programmes. The Jefferson’s Scale of Physician Lifelong Learning (JSPLLL) was used to measure NOLLL among 200 nurses at Uganda’s national hospital. Most of the participants had fair orientation (52%) towards lifelong learning (LLL), with a JSPLLL mean score = 36.8 ± 7.2, and rated their skills in self-directed learning as good or excellent (44%). Reported barriers to LLL were patient work-load, lack of mentors, library resources and computer skills. NOLLL was significantly associated with professional experience (P = 804; 0.05), age (P = 804; 0.05) and education level (P = 0.01). In Uganda, NOLLL is still sub-optimal and this has implications for successful implementation of continuing education programmes for nurses.
Postnatal Exercise Programme on the Health Related Fitness of Omani Primi Postnatal Women
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Despite the fact that exercise is beneficial to the general population and pregnant women specifically, there is insufficient evidence regarding the effect of postnatal exercise on the well-being of Omani women. It may be beneficial to test the hypothesis that postnatal participation in a well-designed exercise programme will enhance Omani women's health. However, there are vast differences between theory and practice in implementing such an experiment in Oman. This paper aims to elaborate the limitations and obstacles facing this type of project. Methods design is crucial to counteract the dilemma of Omani women; they want to be fit but have no sustainable commitment to an exercise programme. The study used a randomised controlled trial design. 50 postnatal women were recruited to the exercise group and 50 to the control group. Selection criteria were based on normal vaginal delivery, willingness to participate, and residence in the Muscat region. Health-related fitness components, both before and after implementation of the exercise programme, were to include handgrip and leg strength tests; aerobic stepping; lower trunk flexibility measurements; calculation of body mass index, and performance in push-up and sit-up tests. In addition, a standardised questionnaire was used to assess both psychological and social wellbeing in the subjects. An exercise programme was recorded and distributed to motivate subjects to work out in their homes. It was anticipated that the Omani women who participated regularly in the exercise programme would have greater health benefits than those women who failed to participate in an exercise regime. However, the investigators found that cultural barriers, plus husband and family customs, may have impeded their participation. Therefore we highlighted the difficulties and barriers faced in accomplishing a postnatal exercise programme. In conclusion, details of the project, its value, limitations, and the process will be presented.

Dietary Intake of High School Students and Factors Affecting the Next Generation of Nurses in the United Kingdom: Findings from a qualitative study
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From September 2012, all students who study to obtain a registration in nursing in the UK will undertake degree level programmes. Nursing in the UK is changing. First, there is a move to change health care, placing more emphasis on community-based care. Second, funding is changing, with budget-holding general practitioners being given more power and freedom to source care within their communities. A recent government paper has also proposed that nurses will coordinate and lead teams in a range of settings. Taken together these can be described as positive drivers for nursing education, allowing an expanded and developed nursing role. There are, however, also a number of negative drivers. In the UK it is likely that the number of students trained to full registration will decrease in the near future. This is worsened by between 25 and 30 percent of students not completing their studies, which is a significant financial drain. Using a grounded theory methodology, a set of semi-structured interviews was conducted throughout the UK with academics who are involved in student selection (N = 14). Enquiry focused on two main areas: personal qualities required for new student nurses and experiences of selection in comparison to procedures. Interviews were recorded, transcribed, and analysed using a constant comparative technique. A number of common themes emerged, the most vivid being a pragmatic concept we have entitled ‘Orientation for Professionalism.’ This is composed of a number of conceptual elements which can be explored and evaluated during the selection process. These findings have been used within De Montfort University through a process of positive reflection to produce a new student selection process which allows sensitive and differentiated assessment of students at the selection phase. Perspectives will be shared regarding the implementation of this into practice.

Serum Lipid Peroxides, Lipids, Antioxidant Defence System of Erythrocytes and Antioxidant Vitamins in Plasma of Urban and Rural Egyptian Men
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Lipid peroxides, which are produced inevitably from polyunsaturated fatty acids, may damage cell membranes and might accelerate cellular ageing. Research results to date indicate that increased levels of lipid peroxides are associated with premature ageing, atherosclerotic process, hypertension, and cancer. Serum lipid peroxides, thiobarbituric acid reactive substances (TBARS), lipids, enzymatic and vitamin antioxidants, blood pressure, body mass index, and dietary intake in 200 urban men were compared with the same number of rural men. The haematological analysis for all subjects indicated that significantly higher levels of TBARS, serum cholesterol and triglycerides (TG) were seen in urban men when compared with the rural men. The opposite was observed for the activities of antioxidant enzymes, glutathione peroxidase, superoxide dismutase, and catalase measured in the erythrocytes and antioxidant vitamins measured in plasma including A, C, and E. Also, significant correlations were observed between TBARS, serum cholesterol, and TG in the urban men. All of these findings suggest that significant elevation of TBARS and lipids and a decrease in antioxidant enzymes and vitamins in urban men may be the result of urbanisation, including exposure to environmental and food pollutants.
A Descriptive Study to Determine the Relationship between Stress Coping Skills and Cognition
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Can the cognition of students be influenced to help them cope with stress? Nurses experience high rates of stress. College students, including nursing students, feel more overwhelmed and stressed than before. Are they equipped with adequate coping skills? This study aimed to assess and compare cognitive styles of nursing students, evaluate and compare their coping skills, and to explore the relationship between cognitive styles and stress coping skills. A cross-sectional descriptive correlational design was used with 443 students (214 first year and 229 final year students pursuing general nursing and midwifery [GNM]). Stress-coping skills were evaluated in its seven dimensions with the coping skills inventory. Six different styles of cognition were assessed with the personal style inventory (test-retest reliability). The difference between the intuitive mode of cognitive style used by the first-year and the logical mode of cognitive style used by the third-year (GNM) students was statistically significant. Also a statistically significant difference exists between first-year and third-year GNM students in some dimensions of coping skills such as reactivity to stress, the ability to relax, and self-reliance. Additionally, there is significant correlation between the cognitive styles and stress-coping skills of students. Stress-coping skills can be positively strengthened and stress can indeed be managed by means of cognitive strengthening. Teachers should try their best to innovatively strengthen the resilience of students.

Jordanian Nurses’ Attitudes towards Organ Donation from Brain Dead Patients in the ICU
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Intensive care unit (ICU) nurses play a major role in the transplantation process, and it is important to study their attitudes as Jordan is experiencing an increase in cadaveric organ donation. No research has been done to assess Jordanian ICU nurses’ attitudes which are influenced by cultural backgrounds, social norms, and religious beliefs. This study explored Jordanian nurses’ attitudes regarding organ donation from brain dead patients in the ICU. The researchers used a cross-sectional descriptive design with a self-report questionnaire, developed by Kim, Fisher & Elliott (2006), with convenience sampling to collect data from 216 ICU nurses from nine private hospitals in Amman, Jordan. The survey period was from March to April 2007. The majority of nurses in our sample (92.6%) accepted brain death as true death. Nevertheless, an obvious decrement (66.2%) is seen when it was related to supporting the donation from the brain dead patients. But when it was related to donating their organs and their family members’ organs, just 55.1% and 36.6%, respectively, agreed with the procedure. ICU experience positively affected nurses’ attitudes in the organ donation process. There is a misunderstanding of the Islamic point of view and following the fatwa of forbiddance among nurses. This research finding provided new insight into Jordanian ICU nurses’ attitudes towards organ donation from brain dead patients. They have, in general, some positive attitudes toward organ donation, but with mixed feelings, especially regarding themselves and their families. These findings could be effectively used in further research.

General Social Function for Elderly in Geriatric Homes
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The study aimed to assess general social factors for the elderly in geriatric homes in Jordan. A sample of 155 residents was selected. The Older Americans Resource and Services (OARS) social resource scale was used for data collection. The questions focused on the facilities’ residents’ family structure, patterns of friends and visiting, availability of a confidant, satisfaction with the degree of social interaction, availability of a helper in the event of illness or disability, and outing programmes. The findings revealed that the life expectancy for women is greater than for men. In respect to marital status, 38.1% of those surveyed were widows. Only 15.5% of them were visited by their family more than 5 times a year. Of respondents, 61.3% trust the home’s staff and 25.1% have friends in the home. In regard to loneliness, 66.5% feel lonely and need outside assistance. In regard to clients’ help, 42% did not know how to answer this question.

Pressure Ulcer Project Initiatives
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This paper presents the pressure ulcers project initiatives at Khoula Hospital. It will highlight implementation of the evidence-based risk assessment tool used for the prevention of pressure ulcers. Within the complex and rapidly
changing health care environment, it is essential that the best available evidence is obtained to inform the practice. The European Pressure Ulcer Advisory Panel (EPUAP) definition is an area of localized damage to the skin and underlying tissue caused by pressure, shear, friction and or a combination of these. They can develop within 2–6 hours as a result of a local breakdown of soft tissue due to compression between a bony prominence and an external surface. This presents a huge burden for families and the health care institutions in any country. The project is located at Khoul Hospital, a National Tertiary Trauma Centre with approximately 485 beds. There were reports of pressure ulcers in patients directly admitted from home, transferred from other institutions or had acquired them during the course of their treatment. Treatment and prevention use significant resources—disposables, equipment, surgery and nursing time. The project group comprised the author, plastic surgeon, dietician, clinical nurses, infection control nurse, social worker and physiotherapist. The main objective was to create awareness and train staff to assess, prevent and manage pressure ulcers. Quarterly workshops were conducted locally and then opened to for any interested institutions including private hospitals. Pressure ulcers are globally considered a quality of care indicator.

A Comparative Study to Assess the Knowledge of Women in Reproductive Age Group Regarding Urinary Tract Infections
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Urinary tract infections (UTIs) affect women more frequently than men, and are among the most common bacterial infections encountered by primary care physicians affecting 20% of women between 15 and 45. 1 woman in 5 develops a UTI during her lifetime and 4 out of 5 women will experience a recurrence of UTI. For women, UTIs are significant health challenges at all stages of life. The study assessed the knowledge of women in urban and rural areas regarding UTIs and compared it to that of women in rural and urban areas, to identify the relationship between this knowledge and selected socio-demographic variables, and to develop a UTI health education module. A simple random sampling technique by lottery method was used. Participants included 75 women from rural areas and 75 from urban areas. Data were collected using a structured interview schedule and analysis done by using descriptive and inferential statistics. In urban areas, 36% of women were very knowledgeable, while in rural areas no women were highly knowledgeable. In urban areas, a significant relationship was found between women’s ages and their level of knowledge, education, occupation, religion, marital status and history of UTIs. In rural areas, there was a significant relationship between their knowledge and education, occupation, caste and marital status. This indicates the need for a health education module to support health awareness campaigns. It will focus on prevention, early detection, and management of UTIs and thus indirectly help reduce the incidence of UTIs.

Fear of Death among Drug Addict Patients
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The primary aim of this study was, to examine the level of death anxiety (thanatophobia) in drug-dependent individuals attending the outpatient clinic in a psychiatric hospital, and to examine the relationship of demographic variables to death anxiety. 65 patients were recruited from outpatients at The Psychiatric Hospital in Bahrain. The death anxiety scale was administered to assess death anxiety, and a clinical psychiatric interview was used to assess psychopathology. The mean age of the sample was 36.8 years (SD 8.8). All subjects who participated in the study were Arabic males; the majority of them were primary school educated (67%) and single (48%; 56.5%). The total mean death anxiety score of the drug abusers was high (3.52 ± .95). One-way analysis of variance (ANOVA) showed that there was no significant difference among the scores the drug dependents received on the death anxiety scale related to different groups of age, education, type of drug used, or the number of times of taking drugs per day. However, there was a significant difference in the level of control of use, marital status, duration of use, cigarette smoking, and level of religiosity. The results of this study indicated that the level of death anxiety is high, in general, among drug abusers and that being divorced, not actively practicing a religious faith, having at least 1–10 years or more than 20 years history of drug abuse, and smoking at least 20 or more cigarettes per day significantly increased the level of death anxiety.

Evaluating the Effectiveness of a Clinical Preceptorship Program for RNs in Jordan
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A shortage of clinical nursing instructors and an absence of hospital staff in clinical teaching may lead to incompetent graduates and poor quality of patient care. This study aimed to design and implement a programme to train registered nurses (RNs) as preceptors, and to set up a nursing preceptorship education programme. True experimental design was utilised. The sample consisted of 68 RNs recruited randomly from governmental, private, and university hospitals. A socio-demographic data form and a questionnaire concerning nurses’ knowledge of preceptorship were developed for self-administration. The study results indicated that the difference between experimental (N=30, M=33/41, SD=4.5) and control (N=38, M=26/41, SD=4.6) groups after implementing
the preceptorship programme is statistically significant (t=5.5, df=66, P <0.001). These results suggest the usefulness of implementing preceptorship educational programmes to improve preceptors’ knowledge regarding teaching strategies. The preceptorship programme significantly improved knowledge of clinical teaching.

### Transforming Education to Strengthen Health Systems: The Lancet Commission Report

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In 1910, the Flexner Report led to a series of studies about the education of health professionals. Today, conspicuous gaps demonstrate a collective global failure in health systems as they struggle to manage complex and expensive demands on health professionals. Professional education in the health sector has not kept up with increasing challenges. Deficits can be seen in the disparity of abilities to meet health consumer needs, health worker shortages, the incongruent theory-practice nexus, a focus on tertiary rather than primary care, imbalances in the labour market, and a failure to improve health systems. Health professions resemble silos, often acting in isolation or even in competition with each other. Remote areas are underserved, and mass migration of health professionals is common, both away from their own countries and from the specialties they trained for. The Lancet Commission (20 professional academic leaders from around the world) took a global, interdisciplinary perspective, and a systematic approach to consider alliances between education and health systems. The Commission concluded that positive health outcomes require new instructional and institutional designs. This presentation discusses reforms in professional health education, as highlighted in the findings from the Lancet Commission’s report, with a specific focus on the impact for nurses, in order to develop a new vision to transform Omani health education.

### Preceptorship: A shared Journey between practice and education

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Clinical teaching is a purposeful facilitation of learning in the clinical setting that includes the identification of learning needs, the establishment of curricular outcomes, arranging and planning learning opportunities, planning and delivering learning experiences, assessment, and feedback and evaluation. Preceptorship is an enabling process structured to support learners in clinical practice to achieve specified outcomes within a stated period of time. Preceptors help students develop a knowledge base and clinical skills, and are described as experienced nurses who facilitate and evaluate student learning in clinical work over a predetermined amount of time, in addition to their regularly assigned nursing functions. Serving as resource people and role models in one-to-one relationships, preceptors introduce students to the nursing role through direct involvement in the teaching-learning process. In 2004, the Nursing Division at the College of Health Sciences in Bahrain developed a preceptor programme that provided opportunities for reflection, critical thinking, and discussions between preceptors and preceptees. It also helped to strengthen clinical learning experiences for students. This presentation summarises the benefits of preceptorship, outlines preceptor responsibilities and qualities, discusses the process of preceptor selection and role preparation, and details the evaluation system in the Bahrain College of Health Sciences.

### First Year Student Nurses Experience a New Beginning through Problem Based Learning

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Nursing education in Ireland and internationally is increasingly under pressure to focus on developing nurses who are equipped to work in a rapidly changing, multicultural environment influenced by fiscal constraints and technological advances. The delivery of health care is becoming more complex and requires that professional nurses are proficient critical thinkers, problem solvers and self-directed learners. Problem-based learning (PBL) is promoted as a means to nurture and facilitate critical thinking and self-directed learning skills among nursing students. The concept of PBL is well-established in the professions of medicine, engineering, law, and nursing in N. America and the UK, and is frequently referred to as a total approach to education. PBL is an innovative student-centred approach that teaches a multitude of strategies critical for success in the 21stcentury. Nurse educators must develop the necessary skills and knowledge to integrate the theory of PBL into the curriculum, and evaluate teaching strategies that successfully prepare knowledgeable, competent, and professional graduates. These qualities are reflected as sound clinical judgements that result in quality care administered by skilled practitioners. This presentation shares lessons learnt from introducing a PBL approach for first-year student nurses. Written case study scenarios presented to a class facilitated transformational learning as the students engaged in self-directed inquiry and critical thinking. Small groups organised the information and identified relevant concepts as they analysed and evaluated all viewpoints. Multiple perspectives from both personal experience and theory enhanced the discussion and students became actively involved with the case scenario, related to authentic professional practice. Nurse education programmes should provide opportunities for students to develop
these skills and abilities.

**Application of Cognitive Critical Thinking Skills in the Nursing Process by Nursing Students**

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Evidence-based nursing practice focuses on the need for nurses to demonstrate orderliness, diligence, patience, reasonableness, persistence, willingness, flexibility, and precision when dealing with health care issues. Student who aspire to become competent nurses are geared by nurse educators to overcome challenges and organise and implement patient care behaviours. Knapp states that ‘it is in the application of nursing process that a nurse becomes proficient at critical thinking’. Literature increasingly points at the need to infuse critical thinking into clinical education scenarios. In clinical nursing education the learner is able to marry the theoretical component with practice using the nursing process approach. This approach is a powerful scientific vehicle to facilitate critical thinking. This study was descriptive. Data were collected using a tool, adapted from Facione’s 1990 Core CCTS. The sub-skills investigated were inference, recognition of assumptions, deduction, interpretation, and evaluation. 60 nursing care plans were drafted by 2 levels of students. The results showed that there were significant differences in the use of CCTS by nursing students. A major theme was that the nursing process compels students to apply CCTS. There was a significant difference in the application of CCTS between the 2 levels of nursing students. When nursing students are helped to identify and integrate CCTS in nursing process, their critical thinking skills become functional and lead to successful implementation in clinical practice.

**The Influence of Academic Nurse Role Ambiguity and Role Conflict on Organisational claimant in Saudi Arabia**

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Higher education in Saudi Arabia (KSA) was established to enhance the nation’s growth and well-being. The KSA’s nursing faculty’s mission covers teaching, research, and community service. The interaction of these factors may influence the academic setting and impact teaching nurses’ roles. This study aimed to examine the influence of academic nurses’ roles, and the ambiguity and role conflicts within institutions in KSA. A non-experimental, descriptive, cross-action correlation was conducted in the KSA’s three oldest and largest universities. Full-time nursing instructors were recruited to participate in the study. All respondents completed the role conflict and role ambiguity scale. In addition, the organisational climate description questionnaire of higher education was used for data collection. Self-reported survey procedures were used to collect the study data. Descriptive procedures and Pearson’s product-moment correlation coefficients were used. The majority of participants were expatriates with a mean age of 36.86 years. The results revealed that the role ambiguity mean of nursing teachers = 29.88 while the role conflict mean = 35.26. In addition, the results showed that intimacy received the lowest mean score in the category of organisational climate. Role ambiguity positively correlated with all dimensions of organisational climate. However, only role conflict positively correlated to disengagement. This result suggested that the nursing faculty faced role conflict and ambiguity. They also suggest that KSA’s nursing faculty have different perceptions of what their roles are compared to their colleagues or dean. Faculty members experience deliberation, disengagement, and lack of intimacy in the academic setting. These findings have negative implications for a healthy workplace. Deans should make an effort to match institutional and individual goals, and open discussions should take place between administrators and faculty about role expectations, criteria for promotion, and other institutional rewards.

**Critical Thinking: Teaching for Saliency and Priority Setting**

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Implementation of critical thinking in caring for patients and their families comes through determining what the needs are, and then prioritising those needs based on saliency, meaning, and determining what is of most importance, or is most urgent now. Setting priorities based on saliency is an acquired behaviour that teachers can teach and students can learn. Teaching strategies that enable the acquisition of these behaviours include building upon prior knowledge, conducting guided inquiry, and reflecting on practice. This session is devoted to expanding and implementing these strategies through case studies and interactive small group discussions.

**Perceptions of Nursing Science Students regarding Factors which Hamper their Motivation**

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This research originated from the observation that the motivation of nursing science students gradually declines during the course of their training. According to the literature, nursing science lecturers play a vital role in motivating their students.
The Influence of a BSc. in Nursing on Professional Practice
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Cardiff University, the Ministry of Health in Oman, and the Oman Specialised Nursing Institute developed a bachelor of science (BSc) in nursing studies for qualified nurses, delivered in Oman. The first cohort commenced in May 2009; a second cohort in September 2010, and a third in September 2011. A longitudinal research study was established to explore nurses’ and managers’ perceptions of the effects of a BSc in nursing on professional development and practice, and to identify factors that influenced the implementation of new learning. Preliminary findings from phase 1 are presented. This qualitative study collected data through focus groups and interviews. One focus group consisted of students nearly having completed the course. Interviews with a random selection of ten students and ten managers took place six months later. Data were transcribed using a ‘template approach’ and emerging themes and findings were agreed upon by a research team. Early results indicate that the BSc has developed the evidence-based practitioner, who is able to search for evidence, critique research, and apply findings to practice. Confidence, leadership, and change management skills improved and many nurses were promoted to senior positions. Factors that inhibited the implementation of new learning were time, staff shortages, the culture of nursing, and resistance by other staff. Facilitating factors included support of managers and a thirst by self and others to further professionalise nursing. Nurses felt able to stand up for the profession and to talk with doctors on the same professional standing. Educating nurses at degree level will develop the individual and further develop nursing as a profession in Oman as well as improve care to patients by evidence-based practice.

Assessing Clinical Learning Environment for Baccalaureate Nursing Students in Muscat
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The quality of the clinical learning environment/placement is an essential factor in determining the quality of nursing students’ clinical experience/ learning. This paper reports an evaluation of the clinical learning environment for baccalaureate nursing students in Oman based on the cognitive and socio-emotional aspects of the learning process. An exploratory study of nursing students’ perceptions of their learning environment was carried out using the clinical learning environment inventory (CLEI) derived from a comprehensive review of literature. After a pilot study, the instrument was administered to 100 undergraduate nursing students from 2 cohorts of the nursing programme in 2011 in Sultan Qaboos University. Inferential statistics and multiple regressions were computed. The students perceived their clinical learning environment as good. Some students were extremely satisfied (90%) with activities done on the ward, while others reported less satisfaction (80%). Most of the students (92%) agreed that practical work experience was useful. Providing an effective and productive clinical experience is vital in preparing nursing students to become competent clinicians. The CLEI offers a useful measure to explore nursing students’ satisfaction with 2 aspects of clinical experience: clinical facilitator support of learning and the clinical learning environment, and is considered useful for assessing learning environments in clinical settings.

Writing-to-Learn as a Learning Strategy: attitude of Omani nursing students
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Writing-to-learn (WTL) is considered an important learning strategy in all disciplines. The nursing curriculum requires documentation in clinical practice, expression of ideas in examination, completion of assignments and projects, and contributing to publications and presentations. The aim of this study was to assess the attitude of Omani nursing students towards writing, and to investigate the relationship between certain demographic variables and attitudes towards writing. This study used a modified WTL attitude scale to generate data on Sultan Qaboos University nursing students’ attitudes towards writing. A convenience sampling technique was used. Quantitative data was generated using a structured questionnaire. The scores on writing as a whole, the writing process, and self-efficacy were generated using SPSS. The results indicate that senior and junior students had a more positive attitude whereas middle level students had negative attitudes towards writing. Although 52% of students had a negative attitude to the writing process, the median was higher in the writing process as compared to the median for self-efficacy. There was a positive co-relation between the scores for the writing process and self-efficacy. The findings of this study suggest that students have a negative attitude towards WTL. Attitudes are learned or organised through experiences; hence, negative attitudes towards writing can be transformed with structured interventions. Through WTL, faculty can help nursing students improve their writing skills and understand the course material, thus encouraging critical thinking.
Evidence and Clinical Decision Making in Nursing
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Evidence based practice (EBP) can be defined as “the practice of health care in which the practitioner systematically finds, appraises, and uses the most current and valid research. Findings as the basis for clinical decision.” Nursing is a challenging profession that requires the ability to make critical decisions every day while taking into consideration many factors, such as the patients’ values and beliefs along with the work environment, the current situation and time factors. Integrating clinical decisions with evidence requires a lot of commitment by nurses. They should be aware of current research and this requires a lot of reading and updating. The majority of nurses have a positive attitude about EBP; however, not all of them are actually applying it for a variety of reasons. First, due to time constraints, nurses lack reading time and claim that they do not have the time to conduct research, or that they have not been provided with proper research resources such as Internet or a library. Second, research shows that nurses lack confidence and initiative. Finally, although many nurses are aware of research related to specific information, they tend to follow old methods unless they have been informed to do otherwise by the nursing administration.

Portfolio in Nurse Education
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Recently, there has been an acceleration of changes in the nursing profession and so nurses find themselves confronted with an explosion of nursing knowledge and increasing complexities in their dynamic profession. Therefore, a significant change is occurring in nursing education as institutions attempt to deal with these complexities. In response, nurses need to integrate theory and practice, and current nursing curricula do encourage self-directed learning, where nurses seek and analyse information that they use. Naturally, portfolios are considered to be the device of choice to prove growing competency and encourage students to take an active role in their learning. The use of portfolios in nursing education is increasing and has become a transferable teaching and learning method that demonstrates students’ progress. This presentation will explore the current conceptualisation of the portfolio in nursing education, its advantages for students, and the challenges for nurse educators.

Paradigm Shift in Nursing Education: An imperative change for the future
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Innovation in nursing education entails nurse educators being challenged to think in new ways and explore new possibilities to prepare the future generation of nurses. In the past 25 years, reforms in nursing education have taken place without changing the substance of the curriculum or the educational paradigm. Studies show evidence of nursing school graduates with limited inferential thinking skills and inadequately prepared in pharmacology, clinical practice, leadership, and the use of patient electronic medical records. Often nurse educators are asked to teach more content, but this simple additive curriculum model that we have followed since the time of Nightingale is not enough to ensure that learning has taken place. There is a strong urge to shift instructional emphasis from content coverage to student learning. The ‘curriculum revolution’ should change the way nursing is taught and learned. In short, a ‘paradigm shift’ is needed to prepare future nurses. Transformations taking place in nursing and nursing education are driven by major socioeconomic factors, and by developments in health care delivery and professional issues unique to nursing. Nurse educators need a deeper understanding of trends in health care and their impact on the nursing education/practice in order to facilitate the paradigm shift in nursing education.

Predictors of Pain Management Satisfaction among Jordanian ICU Patients: An exploratory study
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Many studies have reported the problem of undertreating pain among hospitalised patients especially among ICU patients who experience higher pain levels. Despite patients’ pain management satisfaction receiving significant attention, it has not been fully explored among Jordanian ICU patients. The study aimed to: 1) assess Jordanian ICU patients’ pain characteristics (intensity and interference) and levels of pain management satisfaction, and 2) determine predictors of pain management satisfaction among ICU patients. A descriptive cross-sectional design was utilised using the American Pain Society-Patient Outcome Questionnaire to survey 139 Jordanian ICU patients from different health care sectors in Jordan. Higher levels of pain and pain interferences were reported. However, participants were relatively satisfied with pain management approaches. Also, the results showed a predictive model of three predictors, which accounted for 41% of the variance in participants’ satisfaction with pain management. Time needed to get analgesia had the highest predictive power (Beta = -.480, P = .000), followed by average pain interference (beta = .218, P = .02), and being told about the importance of reporting pain (beta = .198, P = .006). Jordanian ICU patients reported pain levels higher than those reported by previous studies in other countries, but comparable levels of pain management.
satisfaction. This supports the need for a caring attitude in managing patients’ pain reports. The study is among the first pain management studies in Jordan aimed at setting the stage for future research studies. Finally, results can be included in planning pain management strategies and protocols within Jordanian hospitals.

Needs Assessment of Cancer Patients and Development of a Standardised Palliative Care Plan to improve Quality of Life

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Palliative care is a concept of holistic care for patients who need symptom relief during their illness. It seeks to maximise quality of life for patients and families. Perception and level of experience of health care professional may affect the continuity of care. Nurses need written guidelines to enhance their performance and provide quality palliative care. The aim of this study was to develop a standardised care plan based on assessment of palliative needs of cancer patients and evaluate the impact of the implemented care on the quality of care. A convenient sample of adults and paediatric cancer patients were recruited from the palliative care unit and assessed before and after implementation of the care plan at the National Cancer Institute, Cairo University, Egypt. Participants participated in a structured interview completed by the researchers, and were given problems assessment tools, and nursing guidelines and patient self-care instructions. The presentation describes the results of patients’ responses before and after implementation of the care plan, as well as the significant differences in the care provided after using the guidelines in spite of the shortage of staff and workload. Palliative care is important and nursing guidelines and educational resources have a great impact on improving the quality of care provided during the various stages of illness. Teaching tools for patients and families should be adapted to individuals’ needs.

Compliance with Infection Prevention and Control Protocols at Governmental Paediatric Hospitals in the Gaza Governorates

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Nosocomial infection is a significant burden for both patients and health systems. The Palestinian Ministry of Health has adopted the National Infection Prevention and Control (IPC) protocol in 2004, aiming to combat infections among health care providers, clients, and community. However, compliance with the IPC protocols has been poorly assessed. The aim of this study was to assess compliance of health care providers with the IPC protocols in the governmental paediatric hospitals in Gaza in order to decrease childhood morbidity and mortality. The study is a descriptive cross-sectional one that included a self-administered questionnaire for all doctors, nurses, and physiotherapists (N=334); an observation checklists for health care providers’ practices, and for the health facility. The reliability of the instruments was assured and the response rate was 92%. The study revealed the most important reasons for non-compliance with the IPC protocol were absence of education or training programmes (61.5%), lack of knowledge (52.4%), and scarcity of the required supplies (46.9%). Only 2.3% of respondents had a copy of the IPC protocol, while 65.8% did not know about its existence. Only 16.9% of respondents had participated in training sessions about IPC. Of those polled, 66.1% had been exposed to an injury from used needles. The observation checklist for the respondents’ practices revealed lower levels of compliance in the areas of wearing uniforms (86.6%); hand washing (45.9%); wearing gloves (40.7%), and using antiseptic and disinfectant (49.16%). Health facility checklists indicate a lack of some essential equipment and materials such as covered waste containers and heavy duty gloves. The study recommended making IPC protocols available in all hospital departments; intensifying education and training programmes by a highly qualified team, and providing the needed equipment and facilities.

Understanding the Sexuality Issues and Queries of the Adolescent Students of Pune

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The adolescent period is a most important phase, marked by various developmental changes. The adolescent becomes capable of reasoning and abstraction for the first time. This period is marked by rapid physical growth, social and emotional development, and a heightening of sexual and romantic interest in others. Adolescents become more aware of themselves and the world around them. This phase is also marked by changes in the reproductive system, which makes them capable of reproduction. Several studies have indicated that adolescents lack knowledge of sexuality and reproduction. How do adolescents address their own sexuality? What are the different issues that worry them and what type of questions really bother adolescent groups? The aims of this study were to assess the perception of the adolescent students about their sexuality and reproductive health, and to analyse the issues faced by the students about their own sexuality. The cluster random sampling method was used to select adolescent students from four schools in Pune City. The sample selected was 119 students in the 8th standard and divided into 8 focus groups. The findings suggested that the majority of the boys (70%) ask more about sexuality than girls (30%). The issues identified by the students were related to understanding sex and its importance, problems related to sex, homosexuality, reproduction, menstruation,
Pre-Hospital Delays, Cognitive Representations, and Coping Responses to Symptoms of Acute Coronary Syndrome in Male and Female Patients of Oman

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Although women in the Arab Gulf Region have shown greater acute coronary symptoms (ACS) events risk scores and hospital mortality than men, no research attention has been given to how men and women cognitively process and cope with symptoms of ACS to make health care seeking decisions. The aim of this study was to examine differences between men and women in cognitive presentation and coping responses to symptoms of ACS. Data from 131 hospitalised patients for ACS (81 men and 50 women) about pre-hospital delays, cognitive representations of and coping responses to the symptoms of ACS were collected by structured interview. Questions were developed based on the response to a symptoms questionnaire. Women reported longer pre-hospital delays than men but the difference was not statistically significant. They were more likely to have hypertension, perceive themselves as less susceptible to ACS and report a greater number of symptoms than men. The women were also more likely to report dyspnoea, nausea/vomiting, and stomach pain than men. Coping responses used by women were similar to men’s. Men who reported shorter pre-hospital delays were more likely to approach their symptoms in a “wait-and-see” fashion, be free from diabetes, experience neck pain and left arm pain, identify the symptoms as cardiac in origin, not use coping responses, and attempt to relax. In contrast, women who reported shorter pre-hospital delays were more likely to experience sweating, perceive greater overall intensity of symptoms, and report fear of diagnostic procedures as a barrier to early health care seeking. Factors contributing to pre-hospital delays in men are thus different to women. Counselling-educational approaches to shorten pre-hospital delays in women should focus on ACS symptoms, and helping them explore their emotional reactions to the symptoms.

Leadership and its Effect on Institutional Culture: The cornerstone of the changing context of nursing and midwifery in Oman

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Nurses in hospitals and health care institutions in Oman are challenged like never before. There has been a seismic shift in the level of clinical experience at the staff nurse level, coupled with a rapid expansion of the outpatient sector, and a demand on hospitals to provide for growing numbers of higher acuity inpatients. The nursing leadership at all health care organisations has been placed under enormous pressure to resolve complex staffing issues, continue Omanisation, and assure clinical competence. The nursing workforce in most institutions is close to 50% of total staff. This creates an opportunity to impact significantly the culture of the organisation. Long standing research shows that leadership excellence has a direct correlation with the institutional culture, employee satisfaction and achievement of high levels of patient safety. This presentation seeks to explore the major research findings and determine their applicability to the situation in Oman. With properly planned and executed training and development, nursing leaders can significantly improve the culture of health care within Oman’s institutions. With proper leadership, the transformation can lead to the highest levels of career satisfaction, clinical competence and patient safety.

Nursing Staffing in Oman: An approach for estimating the requirements of the 8th health system

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At the beginning of the 21st century, it was found that conspicuous gaps and inequities in health still persisted despite the positive outcomes of patients and population health achieved in Oman. New infectious, environmental, and behavioural risks, at a time of rapid demographic and epidemiological transitions, now threaten all the achievements of a health system which still has to struggle to keep up, placing additional demands on health workers. In light of this, health planners and decision makers have to ensure that an adequate number of suitably skilled medical professionals are in place to meet health needs. Although the number of nurses working in health institutions in Oman increased by about 27-fold within the last 35 years to reach 12,102 in 2009, the nursing profession still suffers from acute shortages, skill-mix imbalances, and misdistribution of personnel. This poses a new challenge for decision makers in Oman, and the question of having the right number, the right skills and the right distribution of nurses to meet the requirements of the 8th 5-year plan for health development is one with which planners are struggling. Various approaches have been proposed, all of which have different assumptions, data requirements, and costs. This paper gives an overview of various approaches for planning nursing staffing, with their advantages and limitations. Moreover, it proposes an integrated approach to estimating nursing requirements in Oman to achieve the goals of the 8th Health Plan, besides estimating several scenarios for future requirements, and identifying efficient ways of providing for them.
Job Satisfaction among Nurses working in the Maternity Hospital in Judah, Saudi Arabia
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Saudi Arabia (KSA) is a fast-developing country with a shortage of well-trained Saudi health personnel, especially females. Overcoming this shortage may take some time. Nursing has traditionally been an unacceptable career option for Saudi nationals. The reasons suggested are the low image/status of nurses, and traditional, cultural, and social values. There is no doubt that the present psycho-sociological conditions militate against the entry of young Saudi women into nursing. This unfavourable situation can be ameliorated by improving the working conditions of nurses and increasing their job satisfaction. This research aimed to study the job satisfaction levels of maternity nurses in Judah Azizia, KSA. A descriptive study was undertaken on a convenience sample of 120 maternity nurses. Data were collected through a self-administered questionnaire from December 2010 to March 2011. The questionnaire consisted of two parts. Part I was comprised of five demographic items. Part II was the Mueller-McCloskey Satisfaction Scale, providing information on job satisfaction among nurses and consisting of 31 items to measure the satisfaction of nurses with administrative services, and with their surrounding circumstances. The response rate was 83%. The maternity nurses were highly satisfied with following aspects: the head nurse, their co-workers, respect of their supervisors, and their capability to control the work. Least satisfaction was expressed regarding maternity leave, writing, research, and publication opportunities, and childcare facilities. There was no statistically significant difference between the degree of satisfaction of nurses working in the maternity hospital and the variables of age, nationality, experience, education level, and marital status. The study concluded that maternity nurses are generally satisfied with nursing as a career choice and they are highly committed to the health care system, but some issues may lead to emotional exhaustion and, possibly, job dissatisfaction.

Dignity: The challenge for nurses in long stay older adult units
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Dignity is seen by health care professions and older people as a basic right. However, the literature highlights the effects of situations where the dignity of older people in long term care settings is compromised. From frequent news reports it would appear that older people suffer from poor care. All nurses who work with older people would claim that they treat them with dignity. Why then does poor practice exist? The challenge of this study was to describe the maintenance and compromising of dignity in older adult long term care settings. Although dignity is a central tenet of nursing, it has not been operationally defined and there is only one tool to measure dignity. Evidence suggests that the health care system has failed to maintain dignity in long stay units for older adults, a factor attributed to the abstract concept of dignity and its precise definition. If nurses are to maintain a patient’s dignity, then nurses must have knowledge of the concept and an awareness of how to deliver care whilst maintaining an older adult’s dignity. The aim of this study was to describe how dignity is evidenced by nurses in older adult units. A quantitative descriptive study of 120 registered general nurses’ perceptions of dignity working in 8 long stay units for the older adult in Ireland. The author completed a preliminary concept analysis resulting in three attributes of dignity being used to develop the questionnaire. The study was analysed using the SPSS Package. Nurses maintained patient’s dignity on long stay units for older adults. However, areas where nurses compromised older patient’s dignity were also highlighted, including dignity being compromised when administering medication, feeding, and toileting and maintaining hygiene. Three intended learning outcomes were featured: 1) Describe how dignity is evidenced by nurses in older adult units; 2) Identify attributes of the concept of dignity; 3) Demonstrate how dignity is maintained and compromised when administering medication, nutrition, and toilet care, and maintaining hygiene in older adult units.

Impact of In-Service Training Program on Operating Room Nurses for Reducing Incidence of Infection
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Infection control nurses are qualified experienced nurses who have taken further courses on infection control. They are there to advise staff on how to prevent cross-infection, care for patients with infectious disease, and to assist in the interpretation of hospital policies and procedures dealing with infection control. They are involved in finding and implementing the latest research on infection control, advising on new products, and updating procedures. They work closely with the microbiology department and the health and safety officer. The aim of this study was to investigate the impact of in-service training programmes on operating room nurses in reducing the incidence of infection at Elmbara Hospital, Egypt. A quasi-experimental research design was utilised in this study which was conducted over 2 months. Data were collected from 200 nurses working in operating rooms. The following were used in data collection: 1) a questionnaire to assess nurses’ knowledge; 2) an observation checklist sheet for the nurses to assess their practice, and 3) a training programme. An improvement in mean knowledge and practice scores were found after implementing the training programme. A positive correlation between nurses’ knowledge and practice scores was found immediately and 2 months after implementation of the training programme (P ≤0.0). A significant relationship was found between complications and patients’ sociodemographic characteristics in regards to age and sex. Implementation of an infection
control training programme resulted in a significant improvement in nurses’ knowledge and practice. Improving nurses’ knowledge and practice can favourably affect infections. Continued nursing education and in-service training programmes should be organised at Elmbara Hospital. It should be equipped with the necessary educational facilities and materials to improve nurses’ knowledge and skills which will result in better patient services and outcomes.

Infection Control: Effect of a Designed Teaching Protocol on Nurses’ Knowledge and Practice Regarding to Haematemesis Patients
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The aim of this study was 1) to design a teaching protocol for nurses working with haematemesis, and 2) to evaluate the effect of implementing the protocol on nurses’ knowledge and practice regarding haematemesis patients. The study’s hypothesis was that 1) the post-mean knowledge scores of nurses who are exposed to a designed teaching protocol will be higher than their pre-mean knowledge scores; 2) the post-mean practice scores of nurses who are exposed to a designed teaching protocol will be higher than their pre-mean practice scores; 3) a positive relationship will exist between knowledge and practice scores obtained by nurses receiving the designed teaching protocol. The study was conducted at the emergency unit of Assiut University Hospital. Data were collected from 50 nurses working in the emergency unit. Tools utilised were a questionnaire sheet to assess nurses’ knowledge in addition to some sociodemographic data; an observation check list sheet to assess nurses’ skills, and a designed teaching protocol. The first and second hypotheses were supported by a sharp improvement in the mean knowledge and practice scores after the application of the teaching protocol. The third hypothesis was supported by a positive correlation between the nurses’ knowledge and practice scores immediately after and 2 months after application of the teaching protocol. Patients with haematemesis and their nurses are at high risk for infection. Effective measures to prevent and reduce infection are needed. Improving nurses’ knowledge and practice can favourably affect the incidence and outcome of haematemesis.

Quality of Life, Stress, and Coping of Nurses Working in Selected Hospitals of Karnataka, India: A pilot study
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Nurses make up the largest single group of health care professionals and are trained to consider patients’ quality of care and life, but seldom their own. They rarely consider that they themselves or others in the profession may need care. Lerner found a significant association between job strain and components of health-related quality of life (QOL). The aim of this study was to determine the QOL, stress, and coping of nurses. Instruments used in this study were a descriptive survey of 100 nurses, a demographic proforma, the WHOQOL-BREF, and the nursing stress scale and ways of coping questionnaire. The majority (83%) were 21–30 years. Of those polled, 86% of the subjects were female, 69% were single, and 70% were from nuclear families. Most subjects were working in intensive care units (17%). The majority (64%) had 1–5 years’ experience while 85% had 1–3 years’ experience in their current area of work. The environmental domain of QOL obtained the highest score (26.61) while social domain obtained the lowest score (11.76). A total of 65% of the subjects had mild stress, while moderate stress was experienced by 34%. The mean stress score (6.87 + 3.09) was high for the nurses in the sub-area of death and dying, followed by workload (6.23 + 3.19). The lowest mean stress score was (2.7 + 1.63) in the area of inadequate preparation. The participants’ mean coping score was high (12.3) for positive reappraisal. No significant association was found between QOL, stress, and selected variables. A significant association was found between stress and area of work, coping and marital status, and monthly income, and area of work. A weak but statistically significant negative relationship was found between QOL and stress. A weak but significant relationship was found between stress and coping. No significant relationship was found between QOL and coping of nurses. QOL is affected by stress experienced by the nurses.

Application of Infection Control Measures to Reduce Maternal Sepsis & Gynaecology in a Teaching Hospital, Wad Medani, Sudan
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This interventional study was conducted in the Obstetrics and Gynaecology Teaching Hospital in Wad Medani, Sudan. This study assessed the effect of a programme targeting the application of infection prevention and control measure on the knowledge, attitudes, and practices of nursing staff, and on the occurrence of sepsis among patient admitted to the hospital between 2003 and 2007. Hospital records were reviewed to identify the leading cause of maternal deaths. Knowledge, attitude, and practices of nursing staff were identified through their standardised pre-test question and observation checklist. The results of the study identified that sepsis, a leading cause of maternal deaths, was responsible for 34% of maternal deaths. The knowledge of respondents related to the standard precautions of hospital infection prevention and control measures improved significantly after a training programme. Prior to the training programme, 15% of respondents indicated having knowledge about hand washing techniques, whereas the percentage of those with proper knowledge about hand washing technique increased to 91% post-training. Respondents’ attitudes towards

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infection control measures and their willingness to use them was positively changed. Shortages of necessary supplies and equipment often impeded the achievement of safe levels of infection control. This shortage could also be due to the absence of supervision by an infection control committee. This study recommended periodic refreshers in the form of in-service training courses for nurses in order to update infection control knowledge and practices.

Blended Teaching & Learning Mode - A success story to address the critical shortage in the nursing industry
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In most parts of the world, nursing education has progressed to higher education; nursing education in Malaysia should head in the same direction. Malaysia needs nurses with critical thinking abilities and the motivation for life-long learning, and with skills in technology, communication, management, collaboration and leadership. Malaysia’s progress from hospital-based training to higher education has been rather slow compared with other countries. The Ministry of Health has mandated that in the future, 10% of nurses will have received tertiary education. Higher education for nurses is not a luxury nowadays, but a necessity. Nurses need to be educated at a higher level in order to equip themselves with the knowledge and skills that will empower them to practice innovatively, creatively, and autonomously. There is a need in Malaysia to establish an institution of higher learning to address these issues. Further there is a need to establish and develop a national capacity for retraining and upgrading registered nurses, medical assistants, and student nurses through blended learning, combining self- and face-to-face instruction delivered in a university-based learning environment supported by remote learning centres (RLC). This means establishing a new, distance education based mode for training/retraining registered nurses and medical assistants. Apart from conventional teaching and training methodologies, the varied modes of distance education technology should be explored to ensure that the right match is found. To ensure success, the approach should bring the education/training to the clients rather than expecting clients to be on campus. The vehicle to ensure success will be the integration of conventional teaching-learning methodology with state of the art technology without compromising the quality of education/training provided. Action learning, constructive learning, project-based learning and also problem-solving learning methods will be helpful.

JIGSAW – An innovative approach to teaching students about cancer in children
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A trial study was conducted to teach students about paediatric cancer through the JIGSAW method, a form of collaborative learning. The objective of the study was to incorporate an innovative approach to make the information more student-friendly. Twenty-six 3rd year nursing students were divided into 5 groups of 5–6 members each. “Cancer–Essential Concepts” was divided into 5 segments: a definition and general characteristics of cancer; classification of cancer; staging of cancer; assessment and lab diagnostic tests, and psychosocial implications. Each group was assigned one segment. The level of knowledge on cancer concepts was assessed through a quiz. On average, 95% of the students scored more than 60% in the post test. They also expressed that this method was very useful, enabled decision making, encouraged group discussion, and that they benefited by sharing knowledge. The students also said that it inculcated in them critical thinking. Therefore it can be concluded that this method is beneficial and can enhance the performance of nursing students.

Study to Assess the Prevalence and Knowledge of Diabetes and Hypertension Among Adults
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The aim of this study was to assess the prevalence and knowledge of diabetes and hypertension among adults, and to find the association between knowledge level and variables were conducted in selected villages of Udupi district. The study subjects were interviewed with a questionnaire tested for validity and reliability. Blood pressure was measured by using a calibrated mercury sphygmomanometer and each individual was screened for diabetes mellitus through the Benedict test. A total of 385 adults were selected by non-probability convenient sampling technique. Data was analysed using descriptive and inferential statistics. Of 385 adults, 27.8% were females and 72.2% had been educated up to the primary level. The majority (82.2%) of the adults were unskilled workers and 96% of them had exposure to mass media. The majority (50.4%) had average knowledge on diabetes mellitus and prevalence was found to be only 5%. The majority (50.6%) of the sample had an average level of knowledge about hypertension and the prevalence of hypertension was 19.5%. Results show that there is no significant association between knowledge and selected variables.
Overweight and Obesity and their Correlates among Jordanian Adolescents
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The aims of this study were to provide current estimates of the prevalence of overweight and obesity among Jordanian adolescents 14 to 17 years of age living in Irbid Governorate, and to determine the factors that are associated with overweight and obesity by using a descriptive correlation cross-sectional design. Body mass index, perceived stress, dietary habits, physical activity, and demographics of 824 Jordanian adolescents living in Irbid were measured through a multistage cluster sampling method. The overall prevalence of overweight and obesity was 19.1% and 6.3%, respectively. The prevalence of overweight and obesity among boys was 17.2% and 5.7%, respectively, and among girls was 21.0% and 7.0%, respectively. Both overweight and obesity rates were higher among girls. Physical activity, mother’s educational level, and number of family members were negatively correlated with overweight and obesity. On the other hand, eating breakfast regularly, mother’s weight, consumption of fried food, and perceived stress level were positively correlated with overweight and obesity. Overweight and obesity are becoming a health problem among both boys and girls in Jordan. Detecting the prevalence and the associated factors of overweight and obesity among adolescents is the first step toward proposing intervention strategies.

Developing an Enquiry Based Learning Template for Higher Education
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There are no basic, clear guidelines for academics to realise criteria for enquiry-based learning (EBL). The aim of this study was to develop an EBL template in order to facilitate conversion from traditional didactic teaching to EBL. An extensive literature review was conducted to extract the critical key elements of a universal template. A qualitative approach of one-to-one interviews with experienced staff in developing/coordinating EBL modules at the University of Manchester (UM) was conducted. Twenty-two staff representing different faculties across UM were interviewed. The questions included: a) motivation for developing EBL (i.e. the decision to convert the course and the process of converting from conventional teaching to EBL); b) development and preparation (i.e. stimulating the students’ enquiry or trigger types); c) evaluation and feedback (i.e. maintaining good practice of the process), and d) the use of a universal template (i.e. what elements would make a useful template). All data was treated anonymously and subjected to content analysis. The template is an innovative approach to higher education teaching, and may enable academics to move easily and conveniently to EBL. Additionally, it will aid the university’s major strategy of enabling EBL methods to be developed widely across higher education institutes.

Effectiveness of Computer Assisted Patient Education on Knowledge and Self-Efficacy
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The aim of this study was to describe how much patients know about rheumatoid arthritis (RA) and what kind of self-efficacy they undertake. The aim was also to evaluate the effectiveness of computer-assisted patient education in terms of knowledge and self-efficacy. An evaluative, one group pre-test/post-test design was used. Data were collected from 76 patients who attended the rheumatology polyclinic at Sultan Qaboos Hospital, Salalah. The Arabic version of the patient knowledge questionnaire (PKQ) and the arthritis self-efficacy scale (ASES) were used at baseline, and after 30 days of teaching. Of the 76 patients studied, 90.8% were females, 29% were between 40 and 49 years, 41% were illiterate, and 79% were unemployed. The mean pre-test score of the PKQ was 10.61 ± 4.16. The subscale of RA general knowledge had a better mean, at 3.58 ± 1.70 than that of the knowledge of drugs (1.74 ± 1.14). The mean pre-test scores of subscales exercise were 2.65 ± 1.28 and that of joint protection and energy conservation was 2.64 ± 1.75; 50% of the sample had average knowledge and 48.6% poor knowledge. The mean pre-test self-efficacy scores for pain, function, and other symptoms were 4.60 ± 1.71, 4.99 ± 1.76, and 4.81 ± 2, respectively. The post-test score of knowledge was 21.69 ± 4.04 and self-efficacy was 7.25 ± 1.46. The Wilcoxon-matched pairs signed-rank test showed that knowledge and self-efficacy improved with patient education (Z = -7.44, P <0.0001; Z = -7.19, P <0.0001, respectively). Correlation of knowledge and self-efficacy was significant (r = 0.31, P = 0.007). Education helps patients become accustomed to living with RA.

A Systematic Review Regarding the Effectiveness of High-Fidelity Computerised Simulation in Nursing Education
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Despite the recent move towards the use of high-fidelity simulation (HFS) in nursing education, it has been available since 1960. The current interest in HFS is due to several factors. Policies towards ‘fitness for practice’, advanced technology, nursing shortages, an increase in the number of nursing students, and patient safety concerns are motivating educators to look for new alternatives. Therefore, the aim of this review is to identify the best evidence for the effectiveness of...
HFS on the knowledge, skill, confidence and critical thinking of pre- and post-registration nursing students. The review includes randomised and non-randomised controlled trials which investigated the effects of simulation on nursing students in their education and learning processes between 2000 and 2009. The participants included pre-registered and post-registered nursing students. The interventions included any study evaluating HFS, all of which were considered for inclusion in the review. The search strategy employed defined search and retrieval methods, with MEDLINE, CINAHL, PubMed, British Nursing Index, Psyc INFO and EMBASE accessed for the period of 2000–2009. Nine papers were assessed by two independent reviewers for methodological quality prior to inclusion in the review. For this purpose, the standardised critical appraisal instruments for evidence of effectiveness were used. Differences of opinion were dealt with by consulting with a third reviewer. Six papers were finally included in the review and were analysed using narrative analysis. HFS could significantly affect the knowledge, skill, and confidence of pre-registered nursing students. In addition, the systematic review indicated HFS can increase the confidence of post-registered nursing students. However, there was no evidence to show that HFS can significantly change the critical thinking of students. Additionally, no evidence was found which investigated the effectiveness of HFS on the knowledge and skill of post-registered nursing students.

Q-Methodology: A combination of qualitative and quantitative methods in Nursing Research
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E-mail: daneshn@mcmaster.ca

Q-methodology is a research method where qualitative data are analysed using quantitative techniques. Although it was introduced by William Stephenson in 1935, it is only now emerging as a widely used method in health research, mainly because of advances in its statistical analysis component. It has the strengths of both qualitative and quantitative methods and can be regarded as a bridge between these two approaches. Q-methodology is usually used where the outcome variable involves assessment of subjectivity, including attitudes, perceptions, feelings and values, life experiences such as stress and quality of life, and intra-individual concerns such as self-esteem, body image, and satisfaction. It is used to identify unique and salient viewpoints as well as shared views, thereby providing unique insights into the richness of human subjectivity. In this workshop, different steps of Q-methodology in health research are explained as applied to a research topic. Participants will have the opportunity to participate actively in the different steps of the research process. Also, some common issues in Q-methodology such as sample size, reliability and validity, and interpretation of the statistical analysis will be discussed.

The Health Research Strategy at the Research Council
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E-mail: ahmed.alshukaili@trc.gov.om

The Research Council (TRC) was established by a Royal Decree in June 2005. In November 2006, work began to prepare the organisational structure and develop a national research strategy for Omani science and technology; this was accomplished in 2007. The objectives of TRC are to build research capacity mechanisms, achieve research excellence, build knowledge transfer and value capture, and to provide an enabling environment for research and innovation. The TRC’s overall health research mission is to build research capabilities in a responsive, evidence-based, cost-effective health care system that promotes healthy lifestyles, encourages preventive medicine, and ensures delivery to all citizens. Also, TRC strives to develop collaborative and multi-disciplinary research in genetics, nanotechnology and biotechnology. The health research strategy at TRC is divided into 8 fields. The first, health care delivery systems research, covers health care systems management; primary, secondary and tertiary health care; pharmaceutical health care and nursing care; and quality assurance and patient care. The second covers human resource development research, while the third covers epidemiological research such as disease and injuries tracking; prevention and control; communicable and non-communicable diseases; environmental and occupational health; accidents and injuries, and public health. The remaining fields are health care financing and economic research, health policy research, medical sciences research, and health studies and medical science research.
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Email: ahmad@arab-health.org; Website: www.arab-health.org

Website: www.cppcongress.com

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Website: http://www.icmh2012.usim.edu.my/website

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Website: www.isshp2012.com/

4–8 September 2012: 30th World Congress of Endourology & SWL 2012 (WCE 2012) Istanbul, Turkey
Website: www.wce2012.org/

Website: http://www.icpa2012.com; Email: paedsramesh@yahoo.com

Website: www.9ga.iapb.org/index.php

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Website: www.abudhabimed.com/Home-Main/

Email: drzillur@gmail.com

5–7 November 2012: 3rd Pan-Arab Rhinology Society Conference. Sultan Qaboos University, Muscat, Oman.
Email: rhinologymana@gmail.com

13–15 November 2012: 18th International Paediatric Conference " Striving Towards Excellence" & 2nd Pan Arab Haematology Conference. Sultan Qaboos University, Muscat, Oman
Website: http://conference.squa.edu.om./pedpanarab; Email: pediatricssquh@gmail.com

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2. Drafting the article or revising it critically
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المجلة الطبية جامعة السلطان قابوس

مسجلة بالفهرس الطبي لمنظمة الصحة العالمية، وتعد المجلة منتدى لتبادل ونشر المعارف الطبية والبحوث بين العاملين في مجال الطبي معترف به عالمياً. أصدرت المجلة أربع مرات في السنة وتوزع مجاناً لكل الكليات والمعاهد الطبية في عمان ودول الخليج ومنطقة شرق أسيا.

المجلة الطبية جامعة السلطان قابوس مجلة وطنية وعالمية محكمة للأبحاث الطبية البايولوجية، تهدف إلى تشجيع وتشجيع البحث الطبي والنشر العلمي في عمان ومناطق الخليج، وتطوير المجلات العلمية في المجال الطبي.

المجلة تنشر مقالاتها على الإنترنت، وتتيح للباحثين نشر البحوث والدراسات العلمية، وتستقبل البحوث من جميع المجالات الطبية والحياتية.

المجلة تحتضن أعضاء مجلس التحرير من جميع أنحاء العالم، وتعتبر من المجلات المشهورة في المجالات الطبية والحياتية.

المجلة تحتوي على مجموعة من القصص المختلفة، تغطي مجالات متعددة من المجال الطبي، وتتضمن مقالات للباحثين من خلال جميع أنحاء العالم.

المجلة تحتكر على تلقي بحوث علمية ناشئة في مجالات الطبية والحياتية، وتتيح للمؤلفين نشر بحوثهم في مقالات مكتوبة باللغة العربية والإنجليزية.

المجلة تحتكر على تقديم فرصة للباحثين لنشر他们的工作成果， وتتيح للمؤلفين نشر بحوثهم في مقالات مكتوبة باللغة العربية والإنجليزية.

المجلة تحتكر على تقديم فرصة للباحثين لنشر بحوثهم في مجالات الطبية والحياتية، وتتيح للمؤلفين نشر بحوثهم في مقالات مكتوبة باللغة العربية والإنجليزية.

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