



# KMJ

## KUWAIT MEDICAL JOURNAL

The Official Journal of The Kuwait Medical Association

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### Book

Roberts NK. The cardiac conducting system and His bundle electrogram. New York, Appleton-Century-Crofts, 1981; 49-56.

### Book chapter

Philips SJ, Whisnam JP. Hypertension and stroke, In: Laragh JH, Bremner BM, editors. *Hypertension: pathophysiology, diagnosis, and management*. 2nd ed. New York: Raven Press; 1995. p 465-478.

### Weblinks

U.S. positions on selected issues at the third negotiating session of the Framework Convention on Tobacco Control. Washington, D.C.: Committee on Government Reform, 2002. (Accessed June 4, 2003, at [http://www.house.gov/reform/min/inves.tobacco/index\\_accord.htm](http://www.house.gov/reform/min/inves.tobacco/index_accord.htm).)

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## Editorial

# Treatment of Recurrent Venous Ulcers – A New Surgical Approach

Jan T Christenson

Venous Surgery Center, Division of Cardiovascular Surgery, University Hospital of Geneva, Geneva, Switzerland

Kuwait Medical Journal 2008, 40 (2): 95-98

Severe venous insufficiency is often associated with therapy resistant or recurrent venous leg ulcers due to either reflux in the deep venous system in combination with a secondary superficial venous reflux (as seen in patients with a post-thrombotic syndrome, PTS) or as primary severe superficial venous insufficiency (SVI) without deep vein reflux or with primary deep venous reflux. It is important to note that an estimated 50% of all venous ulcers are seen in primary varicose vein disease.

Venous ulcer is the most frequent lower-extremity ulceration, and is considered to be the most severe complication of chronic venous disease. It is designated C5 and C6 in the CEAP classification<sup>[1]</sup>. The venous ulcer impairs quality of life and is difficult to treat. An estimated 5-8% of the world's population has venous disease, and 1% has venous ulcers at some point in their life<sup>[2]</sup>. Approximately 4% of people older than 65 years of age have active venous ulcers. Recent epidemiologic studies have shown that severe chronic venous disease, according to the CEAP-classification (C4-C6) is present in 3.6-6.1% in European populations<sup>[3-4]</sup>. In the US more than 20,000 new patients with venous ulcers are treated each year and 12% of them require hospitalization, leading to a large burden on the health service<sup>[5]</sup>. The estimated incidence of severe venous insufficiency in the US is 76/100,000 persons per year and venous ulcers is 18/100,000 persons per year<sup>[6]</sup>. The cost of caring for a leg ulcer has been estimated to be in the range of 20,000 to 25,000 USD/year which amounts to a staggering cost of one billion dollars/year in the US<sup>[7]</sup>. Available data suggests costs are also high throughout Europe and Australia. In addition chronic ulcers are common and the personal suffering is high.

Venous hypertension is thought to be the most important factor in the development of severe chronic venous insufficiency. Venous hypertension may occur either as a result of venous reflux in the superficial or deep venous system, or a combination of the two, or as result of complete or partial venous outflow obstruction. The underlying cause for venous hypertension has been described as primary venous valve reflux (70-80%), congenital (1-3%) and traumatic or deep vein thrombosis (DVT) in 18-25%<sup>[8]</sup>.

The development of venous hypertension triggers a cascade of pathologic events such as reflex cutaneous vasoconstriction, closure of pre-capillary sphincters, leakage of plasma proteins, decreased diffusion of oxygen, stimulation of fibroblasts and tissue fibrosis resulting in tissue hypoxia and lipodermatosclerosis. As a result well recognized symptoms such as leg edema, heaviness, pain and itchiness and signs such as varicose veins, eczema, hyperpigmentation, edema, lipodermatosclerosis and venous ulcers will occur<sup>[9]</sup>.

Increased venous pressure, due to venous reflux, leads to a disturbed Starling equilibrium which not only results in capillary stasis, but moreover may lead to extravasation of liquid into adjacent tissue thus increasing the tissue pressure in limited compartments (increased intramuscular compartment pressure) which compromise the microcirculation<sup>[10]</sup>.

Prior to development of venous ulcers venous stasis result in skin and tissue sclerosis (dermatoliposclerosis). Dermatoliposclerosis affects not only skin and subcutaneous tissue but also involves sclerosis of fascias. When this occurs a second tissue compartment with increased tissue pressure may develop (subcutaneous tissue

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compartment, limited by thickened fascias and inelastic, sclerotic skin) which will have an additional negative impact on skin perfusion. Already in 1986 we reported on increased tissue pressures in patients with chronic venous insufficiency<sup>[11]</sup>.

The complexity of this sequence of events may thus explain why venous ulcers are so difficult to treat by conventional management.

The conventional management of chronic venous insufficiency falls into three categories; conservative treatment, surgical treatment and skin and ulcer care. Conservative treatment and prevention of new ulcers aim at controlling edema and lower venous hypertension often obtained by adequate compression therapy<sup>[12]</sup> and systemic drug therapy, such as micronized purified flavonoid fraction (Daflon®, Servier, Paris, France)<sup>[13]</sup>.

Since approximately 85% of patients with venous leg ulcers have reflux in superficial veins eradication of the superficial reflux is often indicated. Surgical treatment includes eradication of superficial venous reflux and closure of incompetent perforating veins. These veins can be ligated, removed or obliterated by surgery, ultrasound guided foam sclerotherapy and/or endovenous obliteration using either radiofrequency or laser as energy source, with often good initial result<sup>[14]</sup>. If deep venous reflux is persisting deep vein reconstruction for reflux control can be considered. Local skin and ulcer care includes local skin treatment and skin grafting.

As described above the etiology of chronic leg ulcers is multifactorial. Data on the natural course of the disease show that healing rates achieved by conservative methods in clinical trials or in newly established clinics are neither achievable in the whole ulcer population nor sustainable long term<sup>[12]</sup>. Even in the best trials, a quarter to half of all ulcers remained unhealed. Not only are venous leg ulcers difficult to heal with current non-surgical regimens but, more seriously, most of them recur. Callam *et al* have reported that 33% of their study population had never healed their first ulcer and 66% had a series of ulcers. In addition half of the patients studied had had their ulcer disease for more than 10 years, some for virtually their entire life<sup>[15]</sup>. Faced with these data, the massive cost of leg ulcer care becomes understandable.

In the recently published ESCHAR study, long-term results have been reported. The ESCHAR trial compared compression alone with compression therapy plus superficial venous surgery in patients with open or recently healed leg ulcers and superficial venous incompetence<sup>[16]</sup>. This study reported on ulcer healing, ulcer recurrence and ulcer-free time over three or four years. The trial found no significant difference between compression alone and compression plus surgery on ulcer healing

at three years, which is in contrast to a study by Obermeyer *et al* reporting ulcer healing in 87% of patients benefiting from surgery<sup>[17]</sup>. On the other hand the ESCHAR trial revealed that recurrence, which otherwise happens in 25% of patients each year, was almost halved. This beneficial effect was most obvious in patients who had incompetence only affecting the superficial veins or those with segmental deep venous incompetence, in which reflux was found in limited segments of the deep veins without widespread valve failure. These findings correspond well with reports by Danielsson *et al*<sup>[18]</sup> and Puggioni *et al*<sup>[19]</sup>.

It has become quite clear that the management of patients with severe chronic insufficiency with venous ulcers should combine conservative management using compression therapy with superficial venous surgery whenever feasible. In addition, superficial venous surgery and compression will both almost certainly have a role in ulcer prophylaxis.

Let's focus for a moment on the importance of the underlying structures of the skin in patients with venous ulcers. When compartment pressure exceeds recumbent tibial vein pressure, tibial veins may be impaired. Increasing compartment pressure leads to progressive local venous hypertension decreased arteriovenous pressure gradient and cessation of capillary flow which may result in ischemia and necrosis of the skin. Fasciotomy has shown to relieve pain, normalize intramuscular pressure, increase muscle blood flow and skeletal muscle metabolism in chronic anterior tibial compartment syndrome, which might be beneficial for ulcer healing if the intramuscular tissue pressure is high<sup>[20]</sup>.

Surgical procedures for venous ulcer disease with lower limb's fascia as the target structure have a long tradition: In 1912 Kondoleon described resection of broad strip of fascia (lateral skin incision and resection of strip of fascia, 5-7cm long, including superficial adjacent dermal tissue<sup>[21]</sup>. In 1953 Linton published his results of long skin and fascia incision including ligation of perforating veins<sup>[22]</sup>. The problems with these techniques were long OR-time, extensive tissue trauma and healing problems within unhealthy skin that was incised. Subcutaneous fasciotomy was first described 1966 by Rosato and in 1985 Hach reported subcutaneous paratibial fasciotomy as treatment of venous ulcers<sup>[23-24]</sup>. The paratibial subcutaneous fasciotomy avoids the drawbacks of the Kondoleon and Linton operations because it requires only a 1cm skin incision which is placed in healthy skin. The fascia is slit open subcutaneous proximal and distal, thus the fascia is opened under the ulcer itself. Remaining close to the tibial bone avoids vascular and lymphatic lesions and a drain is placed if



necessary followed by postoperative compression.

In a recently published report, tissue pressures, intramuscular and subcutaneous, as well as transcutaneous oxygen tension (TcPO<sub>2</sub>) were measured preoperatively, postoperatively and three months postoperatively in patients with post-thrombotic syndrome (PTS) and in patients with severe primary venous insufficiency (SPVI) all with therapy resistant or recurrent venous leg ulcers<sup>[25]</sup>. All patients underwent surgery with removal of superficial venous reflux. In half the study population subcutaneous paratibial fasciotomy was performed as an additional surgical approach. Many variables between groups such as age, gender, ulcer age, and post-treatment compression were eliminated. Severe chronic venous insufficiency with lipodermatosclerosis and therapy resistant venous leg ulcers had significantly increased tissue pressures compared to normal limbs. It was clearly demonstrated that intramuscular tissue pressures was higher in patients with PTS compared to SPVI and that subcutaneous tissue pressure and TcPO<sub>2</sub> did not differ between the groups. Eradication of "all" superficial reflux decreased subcutaneous tissue pressure over three months postoperatively, but had no impact on intramuscular tissue pressures.

The higher intramuscular tissue pressures in the PTS limbs may explain the resistance to healing that is so often seen in the post-thrombotic limb.

Additional subcutaneous paratibial fasciotomy instantly and significantly lowered tissue pressures in both compartments and increased the TcPO<sub>2</sub> significantly.

Eradication of superficial reflux including incompetent perforating veins results in an ulcer healing rate of 46% compared to 96% if additional subcutaneous fasciotomy was performed<sup>[25]</sup>.

Actuarial freedom from ulcer recurrence when subcutaneous fasciotomy was performed was 83% at two years, which is better than any results previous reported in the literature. Patients with ulcer recurrence had higher intramuscular tissue pressures than patients without ulcer recurrence ( $p < 0.001$ ).

The "new" surgical approach adding subcutaneous paratibial fasciotomy to eradication of superficial reflux in the treatment of patients with therapy resistant or recurrent venous leg ulcers followed by adequate compression therapy and local ulcer care ought to be considered. The treatment of venous ulcer disease seems to be mainly pressure related and with combined surgical and compression therapy resulting in faster ulcer healing and less recurrence, this may also have an important socio-economic impact worth taking into account.

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## Review Article

# Curriculum Change in Kuwait: Some Insights into the Goals, Process and Progress

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## BACKGROUND

The responsibility that medical schools bear for training the next generation of doctors is great. Two men are usually ascribed the greatest influence on this process, Abraham Flexner and William Osler. The former was instrumental in creating a scientific basis for medical education and the latter for cementing a relationship between medical practice and educational institutions. This could be thought of as the two halves of the traditional medical curriculum. Although their time of greatest influence was early in the last century the impact of their thinking lives on today. Little changed within medical education for almost one hundred years until there began a debate that challenged the process being used to create doctors best suited for serving society. In this sense, although led from the Western industrialized world, it has slowly become a global phenomenon.

The first change was a break from the traditional discipline based and departmental driven curriculum to systems based teaching, later to become fully integrated with the introduction of clinical science and early clinical exposure. Many medical schools still retain this strategy. But in the late 1960s Howard S Barrows introduced problem based learning (PBL) at McMaster in Canada<sup>[1]</sup>. At last the yoke of teacher centered learning had been broken, although medical schools did not exactly clamour to embrace the strategy in their own schools. It was much later that adaptations of this strategy began to appear with a plethora of names. Accordingly, a hierarchy of strategies employed with the PBL model has been proposed from its application in a pure form, the original McMaster model, where PBL is central to whole process for study, to what seems most popular today which uses PBL as a complementary strategy, in what are called hybrid curricula

Alongside the developments within medical schools there came quite major changes in education. Learning objectives, for instance, were grounded in educational theory during the 1950s and 60s and would give direction to students and teachers alike<sup>[2]</sup>. But what might have seemed like sound practice was soon to run into controversy due to the over specification of the principles<sup>[3]</sup>. The introduction of outcome based educational principles have polarized some as well<sup>[4,5]</sup>. The reason that outcome based education is favoured by the custodians of professional practice is because of the potentially greater accountability inherent in the process of producing graduates who best suit the needs of the society they will serve<sup>[6,7]</sup>. This sounds reasonable. After all who would buy an expensive car without first knowing what they will get for their money?

Through the 1970s and 80s the drivers of change were largely internal and localized until the document issued by the General Medical Council in the UK took the initiative<sup>[6]</sup>. This was both a stick and carrot for the medical schools in Great Britain because the GMC is the accreditation body. No longer could anyone sit on the sidelines. At the same time as major changes began away from the traditional curricula to more innovative curricula, there was serious consideration given to a core curriculum to solve the problem of content overload so long part of traditional curricula<sup>[7]</sup>. Other important issues were now given priority, such as a greater community emphasis and identifying core clinical competences, skills and procedures, communication skills, ethical and medico-legal practice and a personal responsibility towards continuing medical education<sup>[8]</sup>.

So through the 1990s those schools who had invested in change and successfully introduced modern curricula were publishing their

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experiences<sup>[9-11]</sup>. Some important lessons soon became apparent: the competing commitments on faculty staff, lack of evidence supporting the need for change; and when these had been addressed, clearly articulating the chosen change<sup>[12]</sup>. David Prideaux, long known for his common sense and sanguine argument, even wrote an editorial about how to convey a school's experience of change for wider readership<sup>[13]</sup>. By this time several schools who had successfully introduced their version of a modern curriculum were advising others and offering invaluable insights.

However, there still remained the detractors<sup>[14]</sup>, as would be expected. But it is important to hear the question they ask: what evidence is there that these changes produce better doctors? The problem is how to measure whether one generation of doctors is better than the next, with examination performance<sup>[15]</sup>, or perhaps more important feedback from the students themselves and newly graduated doctors from the innovative curricula<sup>[16-18]</sup>.

Mindful of the foregoing, the academic leadership at the Faculty of Medicine, Kuwait University, took two important steps: in the absence of an international accreditation body they commissioned an informal accreditation process by a highly respected body to determine any shortcomings of the school and its curriculum. Secondly, two institutions of excellence in medical education were asked to assist in the preparation and process, University of Dundee<sup>[10]</sup>, UK and University of Sydney<sup>[19]</sup>, Australia. Principles for change were worked out according to the SPICES model<sup>[20]</sup>. The infrastructure was established to develop the new curriculum with wide representation from the teaching staff. A program of faculty development was initiated and open debate encouraged. Also, in 2006, a Center of Medical of Education was re-established. The new curriculum enrolled its first students for the academic year 2005 - 06.

### The New Curriculum in Kuwait

The curriculum chosen is a case-based PBL hybrid model. The program model is an outcome based education one, articulated through four major themes: Integrated Basic and Clinical Sciences (BCS), Clinical Competence, Professional Development and Behaviour and Public Health. There are core and options study opportunities. The planned learning opportunities are linked by objectives that relate to the Outcome under the four themes. Early clinical exposure is led by a Clinical Skills Program supported by hospital and community visits. The program to be effective is logically structured around an incremental scale of developing generic skills<sup>[21]</sup>.

There is a major shift away from teacher centered learning through didactic lecturing to small group learning, supported by the PBL process and interactive tutorial sessions. The sandwich in the curriculum is a horizontally and vertically integrated organ-system based course of study. This part of the program will initially be supported by the use of study guides<sup>[22]</sup>. Later, these are hoped to be replaced by an electronic curriculum.

The assessment process has been revised, new examination formats introduced and a strategy of both formative and summative assessments with in-course and end-course assessments has been evolved. All the assessments are aligned with the curriculum through the learning objectives. Because of the importance attached to assessment, a continuous program of faculty development is running to equip teaching staff with the necessary skills. The Faculty has successfully applied for membership in the IDEAL Consortium<sup>[23]</sup>, which will provide invaluable resources for assessment. Throughout, a process of program evaluation has been introduced to monitor the implementation of the new curriculum. This is just one important component that will contribute to the quality assurance of the Faculty's endeavours.

The new curriculum is a seven year program divided into three phases: Phase I, three semesters; Phase II, five semesters and Phase III, six semesters. Included in Phase I are the two semesters of university study, similar to the pre-professional program of the old curriculum. The third semester is for the preparation of Phase II studies.

Included in Phase II are the following:

1. Foundation Block (4 weeks)
2. Cardiovascular Module (9 weeks)
3. Respiratory Module (9 weeks)
4. Endocrine Module (9 weeks)
5. Musculoskeletal Module (9 weeks)
6. Neurological Sciences Module (9 weeks)
7. Digestive System Module (9 weeks)
8. Renal Module (9 weeks)
9. Blood and Lymph Module (7 weeks)
10. Integumentary Special System Module (4 weeks)
11. Consolidation Module (4 weeks)
12. Two Electives (4 weeks each)

Students will receive a bachelor of medical science degree by the completion (B.Med.Sc) of the Phase II course, irrespective of whether or not they are admitted to the final phase of the program.

Phase III is under construction and will hope to introduce its own set of innovations to support the main pillars of the curriculum and themes.



## DISCUSSION

How can the curriculum change in Kuwait be justified some may ask. When two such influential bodies as the GMC in the UK and the American AAMC lead the way to change there is good reason to listen<sup>[8,24]</sup>. For the American schools it is not the first time such a reform movement has gripped them<sup>[25]</sup>. One major driver of these reforms is the change in medical practice and the expectations put on doctors as a consequence<sup>[26]</sup>. But it is not just the curriculum that should be reviewed and also made fit for purpose; the assessments often are in need of a greater overhaul<sup>[27]</sup>. Another consideration becoming increasingly important is the declining clinical contact that students have with patients as a result of changing attitudes among the public and reforms in health care<sup>[28]</sup>. However, when the impact of this was tested a surprising result was found proving that success in the graduating examinations was not related the extent of a student's clinical experience or lack of it, rather the use of deep learning styles often developed years before<sup>[29]</sup>.

Surely much of this seems familiar and if that is so the question remains what sort of curriculum should be adopted. The Faculty of Medicine in Kuwait have chosen the hybrid model taking the best of the adaptations for PBL<sup>[19]</sup>, reduced the content overload and introduced many more interactive small group learning opportunities. Importantly more time is given for independent study.

Prejudging the outcome for graduates from a new curriculum may seem a bit like the lottery, but there is information that may be helpful. The University of New Mexico has been a popular source of data when comparisons between the performance of graduates from a conventional and PBL curriculum are being reviewed<sup>[30]</sup>. While conventional teaching favoured students in the basic medical science NBME I examinations, PBL better prepared graduates who then completed specialist training and passed the NBME III examinations. These results can be compared with a much earlier report from Michigan State University College where 908 hours of didactic lectures as preparation were compared with 112 hours given in a problem based curriculum<sup>[31]</sup>. There was no difference in scores or pass rates in NBME I. This is supported by a report from the same period showing that a program in medical sciences using independent study prepared students equally well as a conventional lecture based program for the NBME I examination<sup>[32]</sup>. Using both the USMLE Step 1 and 2 and comparing students from a problem based and traditional lecture based curricula showed no differences over a seven year period, the authors concluded that their results would be reassuring for curricula planners<sup>[33]</sup>.

Interestingly, not only are regular students catered for by a modern curriculum but the high flyers appear to thrive on its opportunities. Another report from a US school with a conventional and PBL track confirmed once again no difference in results between students from both tracks in USMLE Step 1 and Step 2. However, there were clear performance differences favouring the PBL strategy for study in clinical performance, knowledge and clinical reasoning as well as non-cognitive behaviours. In addition PBL students were awarded more honours<sup>[34]</sup>. Geography notwithstanding, curriculum change also offers a chance for renewal with a positive balance on educational impact and outcome<sup>[35]</sup>.

Two further influential papers could not report any consistent differences in knowledge base of graduates from PBL schools compared with those from traditional schools<sup>[36,37]</sup>. However, like many reports in medical education the issues and the way they were presented were all a matter of opinion<sup>[38]</sup>.

Results in examinations are quite one thing, what graduates do in practice may be another. From Manchester University in the UK come two helpful reports<sup>[39,40]</sup>. The first developed a questionnaire to survey medical graduates' own perceptions about their preparedness from a traditional curriculum for their first PRHO posting. The results helped modify some components in the radically new curriculum introduced in 1994, thereby qualifying their first graduates in 1999. The second report presents one set of data from the last graduates of the old curriculum and the first from the new<sup>[40]</sup>. The graduates from the new curriculum "rated their course significantly more effective in 12/19 broad competences and 8/13 specific skills" compared with the graduates' rating from the old curriculum. In one area only did the "new" graduates rate their preparedness lower than the "traditional graduates" in "understanding disease processes". However, the clinical supervisors found no difference. It could be argued that if the results had been reversed there would have been a serious cause for concern, or indeed if the "new" graduates had come from elsewhere and the "old" graduates were still being graduated in Manchester, the need for curricular reform at Manchester would have to have been seriously considered as a necessary remedy.

However well-grounded the argument is for curriculum change there will always need to be safety checks built into the process. Both the ongoing course evaluation program and the in-course assessments should give early feedback on the students' progress through Phase II. The best Kuwaiti students, usually admitted to the medical program, are no less able than their counterparts elsewhere in the world. It is true that their motivation

may be different, but we believe that this has much to do with the failings of the traditional curriculum that is being replaced.

We also believe that the students still in the old curriculum will need special support and encouragement, but there is still time to introduce some of the planned Phase III innovations for those students who entered their clinical studies in 2007-08 academic year.

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## Original Article

# Knowledge and Factors Affecting Breast Self-Examination among Kuwaiti Women

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## ABSTRACT

**Objectives:** To determine the frequency of practicing breast self-examination (BSE) among Kuwaiti females and factors that may influence it

**Design:** Questionnaire based cross-sectional survey

**Setting:** Multi-Ministries Compound, Kuwait

**Subjects:** Data was collected from 966 educated Kuwaiti female volunteers through a self-administered questionnaire.

**Main Outcome Measures:** Data regarding the practice of BSE and factors influencing it

**Results:** Among the study sample 357 (37.0%) were practicing BSE. Their mean age was  $31.6 \pm 8.8$  years. The main reasons for not practicing BSE were fear of cancer discovery (13.5%), forgetfulness and failure to realize its importance (15.3%). Moreover, 28.9% did not know the method of examination and 27.8% wished to learn. Only

21.6% reported that they did BSE practice on monthly basis.

Women aged 20-29 years, married with middle income were insignificantly less likely to practice BSE than other categories. Students were more likely to practice BSE than working ladies (OR = 0.3, 95% CI 0.1-0.7). There was a lower possibility of practicing BSE among women receiving their knowledge from TV / radio, newspapers / magazines and friends / relatives than those receiving from doctors. Moreover, the possibility of not practicing BSE decreased if the main source of knowledge were friends/relatives, nurse, media/newspapers respectively compared to those with no source of information.

**Conclusion:** The frequency of BSE is low. It appears that a health education and training program will improve the rate of correct BSE performance.

KEY WORDS: breast cancer, breast self examination, knowledge, practicing

## INTRODUCTION

Breast cancer is a devastating disease that is rapidly growing in overall incidence in all populations. With one million new cases in the world each year, breast cancer is the commonest malignancy in women and comprises 18% of all female cancers<sup>[1]</sup>.

In the United Kingdom, where the age standardized incidence and mortality is the highest in the world, there are more than 14,000 deaths each year, and the incidence is increasing particularly among women aged 50-64 years<sup>[2]</sup>. In the United States, breast cancer, the second most common cancer among women, accounts for one out of every three cancer diagnoses and 17% of all female cancer deaths<sup>[3-4]</sup>. Breast cancer is the most common cancer among females in Kuwait. It presented as 36.3% of all cancers in Kuwaiti females. The age standardized incidence rate was 44.7 per 100,000 among Kuwaiti

females<sup>[5]</sup>. The large difference in the incidence of disease between Westernized and non-Westernized countries is remarkable<sup>[6]</sup>.

Early detection represents the key approach for reducing mortality from this disease<sup>[7]</sup>. Recommended prevention techniques to reduce breast cancer mortality and morbidity include mammography and clinical breast examination (CBE) for women 40 years of age and older<sup>[3,8]</sup>, and monthly breast self-examination (BSE) for women 20 years of age and older<sup>[3]</sup>.

BSE, a cost-free health practice under women's control, can be practiced by both young and old women<sup>[9]</sup>. Often, breast cancer is detected by women themselves through BSE<sup>[10-11]</sup> or by their partners<sup>[12]</sup>. Women who regularly practice BSE are more likely to detect breast cancer at an early stage<sup>[12]</sup>. Results from the Canadian National Breast Screening Study suggest that the performance of specific BSE

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components may reduce the risk of death from breast cancer<sup>[13]</sup>.

No precise statistics on the incidence and prevalence of breast cancer among Middle Eastern Asian Islamic women are available<sup>[14]</sup>. Hence, it is important to stress the practice of BSE as a complementary tool in efforts to detect breast cancer early. This article specifically focuses on breast cancer screening among Kuwaiti women because little is known about the knowledge level, awareness of breast cancer and BSE in Kuwait and the Arab World. Thus, the aim of this study was to determine the frequency of BSE among Kuwaiti females and to study factors that may influence it.

## SUBJECTS AND METHODS

This was a cross-sectional study of self-reported knowledge and frequency of BSE practice among Kuwaiti women. The target population was all Kuwaiti females attending the multi-ministries compound within a four week period. Subjects who met the following selection criteria were included in the study: (a) 19 years of age or older; (b) Kuwaiti nationality; (c) able to understand, read, and write; (d) no personal history of breast cancer.

The study design can be differentiated into two components. The first was a descriptive one to identify the frequency of BSE practice among Kuwaiti females attending the Multi Ministries Compound in Kuwait city during 2004. The second was a comparative study to detect factors that may affect non-practice of BSE. For this purpose, females who participated in the study were classified into two groups (practicing versus non-practicing BSE).

Because Kuwaiti women were the focus of the study, the Multi Ministries Compound in Kuwait city was chosen as the main location for contact with potential subjects. This compound was chosen because it is the largest governmental building that provides many services to different social classes of the Kuwaiti population.

Announcements were made, and women were asked to attend a meeting at which the study was explained by the primary researcher. Women were informed that their responses would be kept confidential, and code numbers rather than names were assigned to the data. Women also were told that they could withdraw from the study at any time. Involved women received general information about the study and their permission to participate was obtained.

Data were collected from eligible females by a self-administered questionnaire. The surveys were limited to a brief series of questions to encourage participation in the study. Questionnaires were then distributed to the women, and completed questionnaires were collected the same day, or at

a later time that was mutually convenient for both participant and the researcher. Data collection was conducted over a four-week period. The total number of women approached was 1297. Out of them 966 women participated in the study, with a response rate of 74.4%.

The questionnaire started by socio-demographic data (age, marital status, education, occupation, income and number of living children). To assess the knowledge of females about breast cancer and its methods of detection, the questionnaire included ten questions. Five of them were related to knowledge about signs and symptoms of breast cancer (*i.e.*, pain, fissures and laceration of nipples, swelling, discharge, weight loss) and the others were related to best methods of breast cancer detection (*i.e.*, BSE, clinical examination, radiological examination, ultrasonography and biopsy). The knowledge index for these items was calculated for each female by summing the right answers to these ten questions. According to this, the index was divided into three knowledge categories ( $\leq 50\%$  = low,  $> 50\%$  &  $\leq 75\%$  = intermediate and above  $75\%$  = high level). Also, the questionnaire included data about BSE (frequency of BSE, source and quality of information about BSE, best age of practicing BSE)

The questions were administered in Arabic and completed in 30 to 50 minutes. Because only women, who could read and write, were included in the study, participants did not experience a barrier in completion of the questionnaires. Only few women asked for minimal clarification of segments of the questionnaire from the primary investigator.

Analyses were initially carried out to compare between females who did and did not practice BSE using a series of univariate comparisons. For the possible confounding effect of the variables, multiple logistic regression was used for the final analysis to predict factors which may be associated with BSE practice. Univariate differences between both groups were detected by independent t-test for normally distributed continuous variables and Chi square test for qualitative variables. Mann-Whitney test was used to detect difference in the total score between the studied groups.

In multivariate analysis, associations between the study variables and practicing status were expressed in terms of odds ratios (OR) together with 95% confidence intervals (95% CI). All explanatory variables included in the logistic model were categorized into two or more levels (<sup>(R)</sup> = reference category): Age (years):  $< 20^{(R)}$ , 20-29, 30-39,  $\geq 40$ ; Marital status: Single<sup>(R)</sup>, married, widow / divorced; Having children: no<sup>(R)</sup>, yes; Level of education: intermediate level and less<sup>(R)</sup>, secondary, university or higher; Income level/ month:  $< 500$  KD<sup>(R)</sup>, 500-1000 KD,  $> 1000$  KD; Occupation: working<sup>(R)</sup>, house



**Table 1:** Comparison of socio-demographic factors between practitioners and non-practitioners of BSE

Variables	Total sample		Practice BSE		Not practice BSE		p-value
	N = 966		N = 357		N = 609		
	n	%	n	%	n	%	
Age groups							
< 20 Y	58	6.0	11	3.1	47	7.7	p < 0.001
20 - 29	389	40.3	119	33.3	270	44.3	
30-39	345	35.7	144	40.3	201	33.0	
40 & above	174	18.0	83	23.2	91	14.9	
Mean ± SD	31.6 ± 8.8		33.4 ± 8.9		30.5 ± 8.5		p < 0.001
Marital status							
Single	278	28.8	84	23.5	194	31.9	p < 0.017
Married	634	65.6	249	69.7	385	63.2	
Others (divorced & widow)	54	5.6	24	6.8	30	4.9	
Having living children							
No	362	37.5	108	30.3	254	41.7	p < 0.001
Yes	604	62.5	249	69.7	355	58.3	
Educational level							
Intermediate level & below	71	7.4	29	8.1	42	6.9	p > 0.05
Secondary	374	38.7	132	37.0	242	39.7	
University or higher	521	53.9	196	54.9	325	53.4	
Income level/ per month							
< 500 KD#	141	14.6	50	14.0	91	14.9	p < 0.013
500-1000 KD	385	39.9	123	34.5	262	43.0	
> 1000 KD	440	45.5	184	51.5	256	42.0	
Occupation							
Working	770	79.7	295	82.7	475	78.0	p < 0.001
House wife	61	6.3	23	6.3	38	6.2	
Retired	39	4.0	24	6.7	15	2.5	
Student	96	9.9	15	4.2	81	13.3	

\*KD = 2.93 \$ (National Bank of Kuwait)

wife, retired, student; Main source of information about cancer breast: doctor<sup>(R)</sup>, pamphlets, TV / Radio, newspapers / magazines, friends / relatives; Main source of information about BSE: do not know<sup>(R)</sup>, doctor; nurse, media / pamphlets, relatives / friends; Ideal frequency of BSE in their opinion: every month<sup>(R)</sup>, every few months, yearly; Best age to start BSE:  $\geq 20$ <sup>(R)</sup>,  $\geq 30$ ,  $\geq 40$ ; Knowledge score level about breast cancer signs, symptoms and methods of detection: low<sup>(R)</sup>, intermediate, high. Analysis was performed using "SPSS for Windows (9)" statistical package.

## RESULTS

A total number of 966 Kuwaiti females free from breast cancer were eligible and included in the study. Among them, 357 (37%) were performing BSE. The mean age of the study population was  $31.6 \pm 8.8$  years. Income varies in our sample, about 14.6% of the women earned below 500 KD, 39.9% of them earned between 500 -1000 KD, and 45.5% had an income above 1000 KD. The majority of our

sample was working females (79.7%).

Table 1 shows the socio-demographic characteristics of the study population. More than three quarters (76.0%) of our sample was between the age group of 20 - 40 years. Only 6.0% were below the age 20 years and 18.0% were 40 years and above. Most of our sample had secondary and higher education or university and higher education (38.7% and 53.9% respectively).

The main reasons for not performing BSE were, fear of cancer discovery (13.4%), forgetfulness (14.6%), failure to realize the importance of BSE (15.3%) and lack of knowledge about the technique of BSE (28.9%). 27.8% wished to learn the method of BSE (Fig. 1). 21.6% volunteers reported that they performed BSE on a monthly basis, 51.3% did every few months and 27.8% did it rarely or yearly (Fig. 2).

To determine the potential factors that may be associated with BSE practice among Kuwaiti females, a total of 357 ladies performing BSE were compared with 609 not performing BSE. The mean

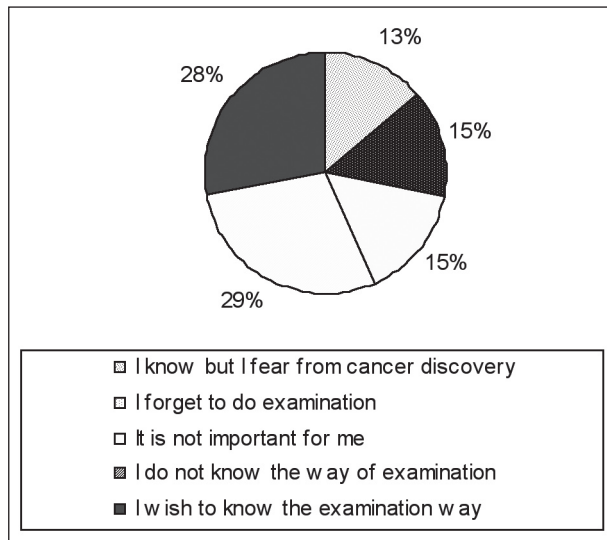


Fig. 1: Reasons for not performing BSE

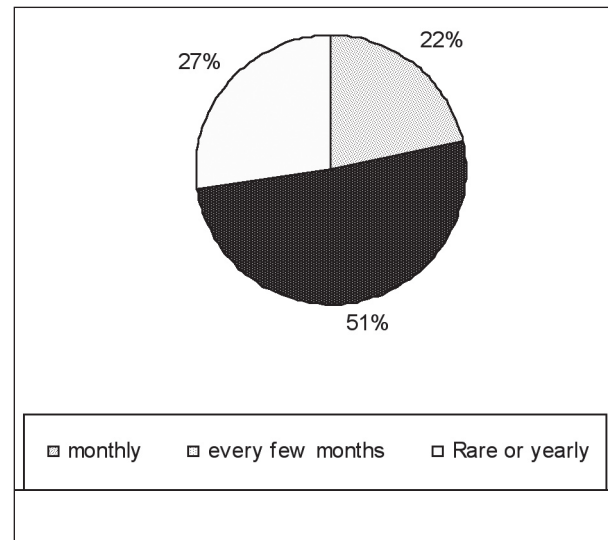


Fig. 2: Rate of BSE practice

Table 2: Comparison of factors influencing BSE between practitioners and non-practitioners

Variables	Total sample N = 966		Practice BSE N = 357		Not practice BSE N = 609		p-value
	n	%	n	%	n	%	
Source of information about cancer breast							
Doctor	24	2.5	14	3.9	10	1.6	p < 0.001
Health pamphlets	92	9.5	38	10.6	54	8.9	
TV & Radio	126	13.0	33	9.2	93	15.3	
Newspapers & magazines	211	21.8	65	18.2	146	24.0	
Friends	513	53.1	207	58.0	306	50.2	
Knowledge about BSE							
Do not know	107	11.1	23	6.4	84	13.8	p < 0.001
Yes I know	859	88.9	334	93.6	525	86.2	
Source of information about method of BSE							
Do not know	107	11.1	23	6.4	84	13.8	p < 0.001
Doctor	198	20.5	98	27.5	100	16.4	
Nurse	26	2.7	11	3.1	15	2.5	
Media & Health pamphlets	261	27.0	83	23.2	178	29.2	
Friends and relatives	374	38.7	142	39.8	232	38.1	
Opinion regarding frequency of practice							
Every month	358	37.1	178	49.9	180	29.6	p < 0.001
Every few months	445	46.1	140	39.2	305	50.1	
Yearly	163	16.9	39	10.9	124	20.4	
Opinion regarding best age for starting BSE							
20 year & above	299	31.0	121	33.9	178	29.2	p < 0.002
30 years & above	438	45.3	174	48.7	264	43.3	
40 years & above	229	23.7	62	17.4	167	27.4	
Knowledge score level							
Low score	267	27.6	63	17.6	204	33.5	p < 0.001
Intermediate score	484	50.1	178	49.9	306	50.2	
higher scores	215	22.3	116	32.5	99	16.3	
Median (IQR)*	6.8 (2.0)		7.2 (2)		6.5 (2.2)		P<0.001**

\* (IQR) = Interquartile range; \*\*Mann-Whitney test; BSE = Breast Self Examination

**Table 3:** Factors predicting BSE practicing: results of multivariate logistic regression analysis

Variable	*OR (95% **CI)
Occupation	
Working®	1
House wife	0.8 (0.4-1.4)
Retired	2.0 (0.9-5.0)
Student	0.3 (0.1-0.7)
Main source of Knowledge about breast cancer	
Doctor®	1
Pamphlets	0.5 (0.2-1.4)
TV & Radio	0.2 (0.1-0.6)
Newspapers & magazines	0.4 (0.1-0.9)
Friends and relatives	0.5 (0.2-0.9)
Main source of Knowledge about BSE	
Do not know®	1
Doctor	1.1 (0.4-2.5)
Nurse	0.5 (0.3-0.8)
Media & Health pamphlets	0.6 (0.4-0.9)
Friends and relatives	0.3(0.2-0.6)
Opinion regarding frequency of BSE	
Every month®	1
Every few months	0.5 (0.4-0.7)
Yearly	0.3 (0.2-0.5)
Opinion regarding best age to start BSE	
20 year & above®	1
30 years & above	0.9 (0.7-1.3)
40 years & above	0.5 (0.3-0.8)
Knowledge score level about BC	
Low knowledge score®	1
Intermediate score	0.3 (0.2-0.5)
High score	0.5 (0.4-0.7)

Variable(s) entered on model, age groups, marital status, having living children, female education, income, occupation, source of information about cancer breast, source of information about BSE, opinion regarding frequency of BSE and best age to start BSE, and knowledge score about breast cancer

® Reference category

\*OR = odds ratio

\*\*CI = confidence interval

age of those practicing BSE was  $33.4 \pm 8.9$  years whereas it was  $30.5 \pm 8.5$  years for non-practitioners. The difference was statistically significant ( $p < 0.001$ ).

The personal and social characteristics together with the results of the univariate analyses are reported in Tables 1 and 2. Women practicing BSE were significantly different from those not practicing as regards age, marital status, having children, income level and occupation. There was no significant difference between both groups regarding education. Moreover, there were statistically significant differences between both groups regarding, main source of information about

breast cancer, knowledge about BSE, main source of information about method of BSE, frequency of BSE practice as well as opinion regarding the best age to start BSE and knowledge score (Table 2).

The results of the final analyses using multiple logistic regressions are summarized in Table 3. Age, marital status, having living children and education were insignificant predictors of non-practicing BSE. Female students were more likely to practice BSE than working females (OR = 0.3, 95% CI: 0.1-0.7).

Concerning the main source of information about breast cancer, multivariate analysis revealed that a higher proportion of non-practitioners of BSE received their knowledge from TV / Radio (OR = 0.2, CI 0.1-0.6), newspapers / magazines (OR = 0.4, CI 0.1-0.9) and friends / relatives (OR = 0.5, CI 0.2-0.9) as compared to those receiving their knowledge from doctors (Table 3). Moreover, the possibility of non practice decreased if the main source of knowledge about BSE was friends / relatives (OR = 0.3, CI 0.2-0.6), nurses (OR = 0.5, CI 0.3-0.8), media / health pamphlets (OR = 0.6, CI 0.4-0.9) compared to those with no source of information

According to subject beliefs, analysis revealed that non-practice of BSE was more among those who thought that the ideal frequency of practicing BSE is once every year (OR = 0.3, CI 0.2-0.5), every few months (OR = 0.5, CI 0.4-0.7) as compared with those who believed in monthly BSE.

Ladies who thought that the best age to start BSE was 40 years and above were less liable to practice BSE than the 20 years and above age group (OR = 0.5, CI 0.3-0.8). As expected, ladies with intermediate or high knowledge scores were more likely to practice BSE than those with lower scores as shown from odds ratios and 95% CI in Table 3.

## DISCUSSION

Unnecessary morbidity and mortality results from breast cancer that could have been prevented and successfully treated if detected earlier<sup>[15]</sup>. By practicing BSE, possible cancer can be detected at an early stage so that health loss for women can be minimized<sup>[16]</sup>.

There is little information available on preventive health practices such as BSE among women in Kuwait. The results of the present study indicate that the majority of Kuwaiti females in the study were knowledgeable about the importance and practice of BSE as a means of early detection of breast cancer. These findings are inconsistent with other studies that indicated lack of awareness regarding breast cancer screening among Asian women<sup>[9,17,18]</sup>. This can be explained by the general characteristics of the selected women. Most of them were of intermediate and high income level and had passed at least the intermediate education or were

students. Thus they may have had access to health care and many sources of knowledge.

Contrary to expectations, this study showed a contradiction between the high proportions of women who know about BSE and believe it to be effective in identifying early breast changes (88.9%), and the relatively low proportion of women who actually perform BSE routinely (37%). Even among those who performed BSE we did not know whether the technique was correct or not. However, 21.6% of them performed it at least once a month. This indicates that there is still a considerable task for health education with respect to spreading awareness about BSE and teaching the correct method. Most women are doing something with respect to BSE, but many seem to be unaware that their BSE is not being carried out correctly.

Coleman reported that, while 96% of the American women had heard about BSE, only 19 - 40% performed BSE on a monthly basis<sup>[12]</sup>. Also, Rosvold *et al* reported that, out of 284 Norwegian women doctors, only 31% performed BSE on a monthly basis and 19% performed BSE less than once every year or not at all<sup>[19]</sup>.

The enormous difference between those knowing about BSE and those performing it indicates that for the majority of women, simply increasing their awareness of BSE is not enough to change their intention and, subsequently, behaviour. This finding goes with other research on early detection of cancer and BSE<sup>[20]</sup> showing that knowledge is an important prerequisite for positive intention and behavior, but in itself often is not ground enough for a positive intention toward early detection behavior.

Our study revealed different reasons for not performing BSE. Women declared that they knew about BSE but were afraid of cancer discovery, were forgetful, did not know the correct method or simply did not realize the importance. This indicates that, next to accurate knowledge, health education should target the psychosocial determinants of performing BSE. Health education should therefore focus on providing women with convincing information that emphasizes the possible positive consequences of BSE and helps them to deal with the possible negative consequences of BSE. Walker *et al* and Rosswurm *et al* reported that if women had cancer they either did not want to know it or were neutral about such knowledge. These women showed less health motivation, did not perceive benefits in doing BSE, and reported barriers to doing BSE<sup>[21,22]</sup>.

Hence direct social support and pressure for performing BSE are very important. Women who feel encouraged by their family, friends, or physician to perform BSE may be more likely to actually do so<sup>[23,24]</sup>. Besides direct support, knowing that other women perform BSE might also encourage women

to do so<sup>[25]</sup>.

In agreement with the findings of Sebahat, and Ilknur in Turkey<sup>[26]</sup>, regression analysis in our study showed that age, marital status, having children, educational and income level were irrelevant predictors of practicing BSE. Actually, demographic characteristics of women have been found to be associated with performing BSE, but the direction and strength of associations have yielded inconsistent findings. Age has been shown to have a positive relationship<sup>[27]</sup>, a negative relationship<sup>[28,29]</sup> or no relationship<sup>[30-33]</sup>. Educational level also has shown to have a positive relationship<sup>[27,34-35]</sup> and no relationship<sup>[31,32,36]</sup>. Therefore, health education is required for all social classes regardless of level of education.

On the other hand, job, main sources of knowledge about breast cancer, BSE, women's opinion about starting age, their opinion about frequency of BSE and knowledge score level were relevant predictors of practicing BSE. Similar results were found in previous studies<sup>[27,28]</sup>.

Our results revealed that the majority of sample thought that the best age to start BSE is 30 years and above. For women under 50, mammography is not considered to be a valid method for detection of breast cancer<sup>[37]</sup>. This means that BSE is the only possible regular early detection method for women younger than 50. Morbidity data show that around 40% of all breast cancers occur before the age of 50<sup>[38]</sup>. This would suggest that BSE, if performed correctly, is a potentially very relevant and useful method.

It was clear that women in this study had access to information about breast cancer and BSE from a variety of sources, and that the majority of those who knew about BSE learned it from sources other than medical professionals, particularly friends. It is possible that having friends performing BSE heightens one's awareness of the importance of early detection. This result supports finding of other studies in which social networks were found to be positive factors influencing different cancer screening behaviours<sup>[39-41]</sup>. In our study, since most of the volunteers worked outside home, were students and were reasonably well educated, they were more likely to be part of social networks that have access to medical information pertaining to BSE.

In the present study, physicians were not the main source of information. This may be explained by the presence of barriers in patient-physician communication that might have hindered the dissemination of information by health care professionals to women<sup>[14,42-43]</sup>. In Kuwait, practitioners are from different nationalities and hence, they may be reticent about asking questions and providing information to women because



of limited knowledge about their cultural and religious practices<sup>[14]</sup>. Physicians are less likely to share information with individuals they perceive to be different from themselves in terms of gender, social class, ethnicity and age<sup>[44]</sup>.

In addition, this study found that only 2.7% of females received their information about BSE from nurses. This result goes with findings of other studies in which nurses do not routinely teach BSE to their female clients<sup>[35,45-46]</sup>. As expected women who were categorized with higher knowledge score were more liable to practice BSE which again enhances the importance of supplying knowledge.

### Limitations:

This study had several limitations. The use of self-reports have intrinsic limitations. People may not understand an item, misinterpret it, or answer the way they believe they should. The selection of educated females limits the generalization of the findings and a more representative sample of Kuwaiti women might be done in the future. The knowledge scale may not be sensitive to women's advanced knowledge of breast cancer and screening. Therefore, additional work needs to be done to develop a more appropriate and reliable knowledge test. Finally, reports of doing BSE do not give information on whether the proper procedure is used.

### CONCLUSION

In conclusion, it may be said from the current study that the rate of BSE performance is low, the main factors affecting BSE are occupation, friends and relatives as a source of knowledge about breast cancer or BSE, their opinions regarding best age to start examination and level of their knowledge about breast cancer.

We recommend that a health education and training program will increase the likelihood of regular BSE performance with a correct technique. Furthermore, education should provide useful suggestions that help women to start performing correct BSE despite possible difficulties. In order to achieve this, it probably would be best to start educating women on performing regular BSE in early adulthood so that this becomes their habitual behavior.

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## Original Article

# Attitudes of General Practitioners towards Cause and Management of Patients with Medically Unexplained Symptoms; Capital Health District, Kuwait

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## ABSTRACT

**Objective:** To survey the attitudes of general practitioners towards management of medically unexplained symptoms in the Capital health region in Kuwait

**Design:** Cross-sectional descriptive study

**Setting:** All primary health care centers under the Capital health region, Kuwait

**Subjects:** All general practitioners (GPs, n = 147) in the included region were surveyed using a self-administered questionnaire.

**Main Outcome Measures:** Respondents' attitudes towards diagnosing and managing patients with medically unexplained symptoms

**Results:** A total of 114 questionnaires were completed and returned giving a response rate of 77.6%. Although the majority of the surveyed physicians declared that patients with medically unexplained symptoms are difficult to manage, most of them felt that they should be

managed in primary care setting. Providing reassurance, counseling and preventing unnecessary investigation were considered important functions of GPs. More than half of the physicians (57%) felt that patients with medically unexplained symptoms have personality problems and more than one third (35.1%) felt that they have psychiatric illness. More than half (55.3%) of the respondents agreed that there are effective treatments for somatization.

**Conclusion:** Despite the fact that GPs consider the management of patients with medically unexplained symptoms an important part of their work responsibility, there is a perception that effective management strategies are lacking. GPs should improve their skills in managing patients with psychosocial problems through continuous medical training programs with the help of psychiatrists.

KEY WORDS: attitude, general practitioner, medically unexplained symptoms

## INTRODUCTION

Medically unexplained symptoms (MUS) present one of the most common problems in modern medical practice accounting for as many as one in five new consultations in primary care<sup>[1,2]</sup>. Headache, fatigue and backache are examples of these symptoms and are considered as a manifestation of somatization. The term somatization is defined as a tendency to experience and communicate somatic distress and symptoms unaccounted for by pathological findings to attribute them to physical illness and to seek medical help for them. Accordingly, the term somatization is used synonymously with the term "medically unexplained symptoms"<sup>[3]</sup>. Patients with somatoform disorders have been consistently demonstrated to experience significant levels of psychological disability as well as high levels of medical costs<sup>[4-6]</sup>. In addition, they have been found difficult to manage<sup>[7-9]</sup>. Poor general practitioner

attitude towards psychological issues was one of the reported predictors of this difficulty<sup>[10]</sup>.

Some patients continue to experience symptoms which become persistent and disabling regardless of reassurance and explanation that they do not represent underlying organic diseases. Any further investigations and reassurance often proves ineffective and the main burden of care falls upon the general practitioners (GPs)<sup>[11]</sup>. Although the central role of GPs in the management of these patients has been emphasized repeatedly, they often express their frustration in dealing with them<sup>[2,12,13]</sup>. A negative attitude, missed diagnoses and lack of treatment not only frustrate GPs but may also affect patient care<sup>[14]</sup>. Nevertheless, most GPs believe that these patients should be managed in primary care<sup>[13]</sup>.

The amount of ongoing research in this area has increased dramatically during the past 15 years<sup>[15]</sup>. This is an indication of the increasing recognition

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that physical symptoms and psychiatric disorders are often linked and that the consideration of one without the other may hinder any form of treatment<sup>[16]</sup>. Most studies were interested in studying somatoform disorders in terms of classification and explanation of the syndrome but there has been little consideration of the attitudes of GPs towards these patients<sup>[11]</sup>.

This study aimed to survey the attitude of GPs towards diagnosis and management of patients with MUS in the Capital health region in Kuwait.

## SUBJECTS AND METHODS

The healthcare system in Kuwait is divided into five regional health authorities. Primary healthcare is provided by 77 primary health care centers served by either family medicine practitioners (FMPs) or GPs. The capital health region served about 474,600 inhabitants in 2005 with 184 primary healthcare physicians in 21 centers. Thirty seven physicians work in maternal care and diabetic care centers. The remaining 147 physicians work in the other primary healthcare centers. Out of them 58 were qualified as FMPs. Kuwaitis represented 80% of the family practice qualified physicians and 32% out of the GPs.

A cross-sectional survey was conducted from January to April 2006 including all GPs working in the primary health care centers at the Capital health region. A self-administered questionnaire was distributed to 147 GPs after obtaining their verbal consent to participate. In order to maintain confidentiality, questionnaires were made anonymous. Out of 147 questionnaires, 114 were returned giving a response rate of 77.6%. The non-response rate was mainly attributed to lack of time due to their heavy work load, lack of interest or non-cooperation.

The questionnaire consisted of six sections: 1) Socio-demographic characteristics: age, gender, years of experience; 2) Attitudes of GPs towards patients with MUS: Are they difficult to manage? Do they have undiagnosed physical illness? Do they have personality problems? Do they have a psychiatric disorders?; 3) Role of GPs in managing patients with MUS: Providing reassurance and support, prescribing psychotropic medications, preventing further inappropriate investigation, providing counseling and psychological management, no involvement at all; 4) GPs opinion about the most appropriate setting for managing MUS; 5) GPs' attitudes towards somatization as a helpful diagnosis; and 6) The view of GPs about the availability of effective treatment for somatization.

GPs responses to sections 2 to 6 were assessed using a 4 – point Likert type scale (strongly agree-

**Table 1:** Gender, age and years of experience of GPs included in this study

Variables (in years)	Male (N = 47)		Female (N = 67)		Total (N = 114)		P- value*
	n	%	n	%	n	%	
Age:							
25 - 34	18	38.3	28	41.8	46	40.4	0.07
35 - 44	12	25.5	27	40.3	39	34.2	
45 - 65	17	36.2	12	17.9	29	25.4	
Experience:							
1 - 10	18	38.3	34	50.7	52	45.6	0.03
11 - 20	13	27.7	24	35.8	37	32.5	
21 - 40	16	34.0	9	13.4	25	21.9	

\*: Chi square test

agree- disagree- strongly disagree).

Data were keyed in a computer and the Statistical Package for Social Sciences (SPSS) version 13 was used for data processing.

Frequencies and percentages in various categories of the Likert scale were presented. Chi-square test was used to detect association between categorical variables. A value of  $p < 0.05$  was considered statistically significant.

## RESULTS

Of the respondents, 41.2% were male. The mean age of the included GPs was  $38.7 \pm 8.4$  years. The mean duration of experience was  $13.8 \pm 8.0$  years. Overall, males were older than females. The majority (82.1%) of females were younger than 45 years while more than one third of males (36.2%) were older than 45 years, a difference that was not statistically significant. Also, males had longer duration of experience than females. One third (34%) of males had experience above 20 years while the majority of females (86.3%) had 20 or less years of experience. This difference was statistically significant (Table 1).

Table 2 shows the attitudes of the respondents towards the diagnosis and the management of patients with MUS. Overall, the majority of the respondents (71.9%) agreed that it was difficult to manage patients with MU and, more than half (57%) agreed that these patients have undiagnosed physical illness. Similarly, more than half (57%) agreed that these patients have personality problems and almost more than a third (35%) agreed that MUS patients have a psychiatric illness. When comparing respondents' view of the GPs role in the management of these patients, it was clear that the majority (98.2%) agreed on their role in providing reassurance and support, whereas 87.7% agreed on providing counseling and psychotherapy for these patients and 78.9% agreed on their role for preventing further investigations. On the other



**Table 2:** GPs' attitude and opinion towards diagnosis and management of MUS patients (percentage of those who agreed on each statement are presented)

GPs attitude and opinion	Years of experience					Age in years			Gender		p-value*	
	Overall N = 114	0 - 10 n = 52	11- 20 n = 37	> 20 n = 25	p-value*	25 - 34 n = 46	34 - 44 n = 39	≥ 45 n = 29	Male n = 47	Females n = 67		
<b>Attitudes towards MUS patients</b>												
They are difficult to manage	71.9	76.9	67.6	68.0	0.55	78.3	71.8	62.0	0.32	78.7	67.0	0.18
They have undiagnosed physical illness	57.0	61.5	46.0	64.0	0.25	60.9	46.2	65.5	0.22	57.4	56.7	0.94
They have personality problem	57.0	50.0	59.5	68.0	0.31	50.0	64.1	68.6	0.42	58.6	44.8	0.40
They have psychiatric illness	35.1	38.5	35.0	28.0	0.17	32.6	38.5	34.5	0.85	25.5	41.8	0.07
<b>Role of GPs in managing MUS patients</b>												
Providing reassurance and support	98.2	98.0	97.3	100.0	0.72	97.8	97.4	100.0	0.70	100.0	97.0	0.23
Preventing further investigations	78.9	84.6	67.6	84.0	0.12	87.0	26.7	82.8	0.06	80.9	77.6	0.68
Providing counseling and psychotherapy	87.7	80.8	89.2	100.0	0.05	82.6	89.5	96.6	0.20	91.5	85.0	0.30
Prescribing psychotropic medications	25.4	26.9	24.3	28.0	0.94	26.1	23.0	31.0	0.76	34.0	20.9	0.12
No involvement at all	2.6	0.0	5.4	4.0	----	0.0	5.1	3.4	----	4.2	1.5	----
<b>The most appropriate setting for managing of MUS patients</b>												
Primary Care	72.2	57.7	75.7	88.0		56.5	76.9	82.8		72.3	68.7	
Medical or Surgical out patient clinic	14.0	17.3	16.2	4.0	0.04	19.6	12.8	6.9	0.11	14.9	13.4	0.76
Psychiatric (Mental Health ) Clinic	15.8	15.0	8.1	8.0		23.9	10.3	10.3		12.8	17.9	
Concept of somatization is helpful in diagnosis	78.1	80.8	78.4	72.0	0.68	78.3	82.1	72.4	0.64	76.6	79.1	0.75
Effective treatment for somatization is available	55.3	48.0	67.6	52.0	0.18	52.17	61.5	51.7	0.62	57.4	53.7	0.70

\*: Chi square test

hand, only 25.4% of them agreed on their role in prescribing psychotropic medication and only 2.6% felt that they should not be involved at all in their management. Of the respondents 80% agreed that primary care is the appropriate setting for the management of these patients, only 16% preferred to refer them to medical and surgical outpatient clinics and 18% of GPs said that psychiatric setting was optimal for treatment of MUS patients.

Although 78.1% of GPs agreed about the usefulness of considering somatization in diagnosis of MUS, only 55.3% felt that there were effective treatments for somatization.

Comparing GPs attitudes and opinions about management of MUS patients according to years of experience, age and gender revealed no statistically significant differences except for GPs opinion about the optimal setting for managing these patients. GPs with more experience found it appropriate to manage patients with MUS in primary health settings ( $p = 0.04$ ).

## DISCUSSION

The majority of the included GPs in this study agreed on the difficulty they encounter when managing patients with MUS. This finding agrees with that of other studies<sup>[7-9]</sup>. This difficulty might have reflected on the referral pattern to medical or surgical outpatient settings. In this study, more than half of the GPs reported their worries of missing physical illness among MUS patients that may be a reflection of the concern of missing diagnosis in the face of increasing medical litigation<sup>[11]</sup>. Also, we found that 57% of the respondents agreed on the contribution of personality factors to the development of somatoform disorders; and only 35% agreed on the existence of psychiatric illness in patients with these disorders. Reasons for this are numerous. They include failure to make a diagnosis of MUS by GPs and the reluctance of some patients to consider psychosocial aspects of their illness. Previous studies suggested that, despite the awareness of relevant social and psychological factors, GPs frequently feel satisfied when these patients express their belief in a physical cause for their symptoms. By arranging investigations, specialists referral and symptomatic treatment, GPs reinforce discrepancies rather than provide different explanations<sup>[17]</sup>.

It was evident that the majority of respondents agreed that primary care is the most appropriate setting for management of patients with MUS. This was much in accordance to the findings of a similar study conducted by Steven Reid<sup>[11]</sup>. Referral to psychiatrists was, however, thought to be a less effective management option. This may be explained not only by patients considering psychosocial

aspects as a contributor to their symptoms but also by the reluctance of general psychiatrists who may focus their attention on psychotic and severe mental illnesses shifting away from non-psychotic disorders. This may result from being less skilled in managing patients with non-psychotic illnesses. In addition, lack of communication between GPs and psychiatrists may be a contributing factor resulting in lack of a clear protocol and plan of management for these patients<sup>[11]</sup>.

The majority of GPs agreed on their role of providing reassurance, support counseling and psychotherapy as well as preventing further investigations. The majority of the respondents, however, did not agree on their role on prescribing psychotropic medication that contrasts with the evidence of the benefits of anti-depressants in some patients of MUS. This could be explained by lack of experience, knowledge or training of GPs to use such medications. Also, the non-availability or the limited variety of such medication at primary care level might be a contributing factor.

Although advances have been made in the understanding of somatoform disorders, large gaps of knowledge in the area of classification and etiology persist<sup>[14]</sup>. In our study, the majority of respondents (78.1%) felt that somatization was a useful diagnosis which was similar to the findings of Steven Reid<sup>[11]</sup>. Despite this, only 55.3% believed in the availability of effective treatment for such patients.

It was evident that a higher proportion of the more experienced GPs thought that primary care is the optimal setting for managing patients with MUS than the less experienced GPs. This may be due to their confidence in their skills in managing such patients.

There are some limitations of this study that may be considered on interpreting these findings. Firstly, although the response rate was high in comparison with similar studies in primary care<sup>[16,17]</sup>, the non-respondent group, however, might have different attitudes towards diagnosis and management of these patients. Secondly, results cannot be generalized to Kuwait since the study was restricted to one health region. Thirdly, it is important to note that this study was a survey of GPs attitudes, which does not necessarily reflect their practice. Also, the effect of family medicine qualification has not been taken into consideration in this study that would have an effect on the attitude of the physicians and that might have the same effect as that of the years of experience or even more. Last and not least, it should be also noted that within the constraints of the questionnaire, understanding the particular aspects in the physician-patient relationship could not be explained. A further study using a qualitative methodology would be of value in addressing

questions such as the GPs anger and being interested in managing patients with MUS.

### CONCLUSION

This study is a further evidence of what most GPs consider that patients with MUS should be managed in primary care and that GPs should provide reassurance, counseling, support and prevent unnecessary investigations for these patients. Despite this fact, there is still a worry that physical illness may pass undetected and there is a perception that effective management strategies are lacking. There is, however, evidence that both recognition and management of mental disorders at primary care level could be improved<sup>[18,19]</sup>.

The traditional post-graduate educational system, by which practitioners maintain and update their knowledge and skills, has been criticized for not being effective or relevant to their educational needs. Further research should aim at identifying GPs' specific educational needs in the area of mental health and patients with MUS as first stage in developing and evaluating programs of training package relevant to those needs. Continuous Medical Education as an important tool in maintaining and improving standards is more likely to be successful if the content is derived from the educational needs of the proposed participants<sup>[20]</sup>. A short multi-faceted training program is expected to produce a change in GPs attitudes towards somatization making them more confident and less frustrated when managing patients with MUS. Psychiatrists need to be proactive in the provision of support and training for GPs in this area as well as emphasizing the importance of psychological and social factors as well as physical factors in illness<sup>[13]</sup>.

Future research would gain from larger studies on GPs attitude changes in relation to somatization. It should also look at the impact of such changes on the doctor-patient interaction and patient care. Also, a comparative study is required to assess the effect of family practice qualification on the attitude of the physicians towards MUS.

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## Original Article

# Red Blood Cell Alloimmunization among Saudi Pregnant Women in the Central Province of Saudi Arabia

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## ABSTRACT

**Objectives:** To determine the incidence of alloimmunization among pregnant women in Saudi Arabia

**Design:** Prospective study

**Setting:** King Khaled University, Hospital, Riyadh, Saudi Arabia

**Subjects:** One thousand one hundred and ninety five pregnant women

**Main Outcome Measures:** The rates of alloimmunization among pregnant women subjects by analyzing the blood type of both mother and neonate

**Results:** The largest fraction of alloimmunization involved Rh antigens (52.38%), while other groups such as Kell & Duffy play a less common role. Alloantibodies identified five types of alloantibodies in addition to nonspecific-autoantibodies. The most frequent (52.38%) were against Rhesus 2.38%; Kell 2.38%; Duffy 2.38%; 4.76% were non-

specific antibodies and 33.3% were autoantibodies.

Alloimmunization are: anti-D 28.57%, anti-C 4.76% anti-E 14.28% and anti-e 4.76%; only one 2.38% developed anti-K; anti-Jk, one 2.38%; one had anti-Le 2.38%; there was one 2.38% with anti-Fy. 1.84% of the total number of study subjects were alloimmunized by antigens of Rh while 0.08% were alloimmunized to antigens either from Kell, Kidd, Lewis or Duffy.

**Conclusions:** The relative importance of antigens other than Rh D have increased since the introduction of Rh D prophylactic treatment. Alloimmunization to E, c and Kell antigens can reach significant proportions of studied populations and can result in deleterious effects on fetus. The actual risk of alloantibody production during pregnancy is unknown but stimuli for antibody production are feto-maternal bleeds that occur throughout pregnancy.

KEY WORDS: alloimmunization, ABO, autoimmune hemolysis, erythroblastosis fetalis, IgG, IgM, Rh

## INTRODUCTION

The overall incidence of hemolytic disease of the newborn (HDN) varies in different places ranging from as low as 7.2/10,000 births to as high as 14.4/10,000 births. Despite prophylactic use of rhesus immune globulin, anti-D is still a common antibody identified in 20% of pregnant women<sup>[1]</sup>. The incidence of anti-D alloimmunization in the weak D (Du) population is closer to that of the D-negative than the D-positive population because few Du patients are of the 'partial' D or Du type.

There are more than 43 other Rh red blood cell antigens which have been implicated in hemolytic disease of the newborn. Anti-C and anti-D are the most frequent antibodies identified in gravid women. Seventy-four percent of infants born to C-alloimmunized women mated to C-positive men show serologic evidence of HDN<sup>[2]</sup>. Pregnancies where the maternal anti-C titer remains at or below 1:16 proceed to final term. Fifty percent of alloimmunized pregnant women need blood

transfusion. Anti-C, Ce alloimmunization is relatively rare. A study in Manitoba, Canada spanning a period of 37 years recorded 11 cases of anti-Cw, and in a review of 131,898 Rhesus positive pregnant women screened for irregular antibodies, the overall incidence was 1:330. Thirty infants in the series required exchange transfusions for HDN<sup>[3]</sup>.

Mothers subjected to unnecessary blood transfusions can produce alloantibodies such as anti-E and anti-Jkb and develop delayed transfusion reactions. Anti-E is found frequently in pregnancy<sup>[4]</sup>.

Majority of Kell sensitization cases are secondary to incompatible red blood cell transfusions since blood is not routinely cross-matched for the Kell antigen. Anti-Kell antibodies are encountered in reproductive women about 60% as often as Rho antibodies but the risk of disease is less than 5% when such antibodies are detected. Anti-k alloimmunization is very rare<sup>[5]</sup>.

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Lewis antibodies are the commonest single cause of positive results in pre-transfusion antibody screening tests. However, the strength of Lewis antibodies is clinically important: Lewis antigens in the plasma of incompatible blood will completely neutralize antibody of low titer. In addition, Lewis antibodies are mostly IgM and red blood cells of newborn infants react only weakly or not at all with Lewis antibodies<sup>[6]</sup>.

Young-Owens and co-workers in 1997<sup>[7]</sup> showed that the prevalence of anti-M isoimmunization may be increasing; the incidence of severe HDN due to anti-M is extremely low and the obstetric concern for the presence of detectable anti-M is only reserved for rising titers. Both anti-M and anti-N react significantly only when the target antigen is present in double dose, *i.e.*, MM or NN.

Antibodies to S, s and U occur following RBC stimulation and are capable of hemolytic transfusion reactions and HDN. Anti-S occurs as infrequently as anti-N while anti-s is rare. Anti-U hemolytic reaction is a diagnosis of exclusion.

Lutheran system antibodies are very rare and can occur in the absence of RBC stimulation. However, they are poorly developed at birth and have not been reported as a cause of HDN. Anti-Fya and anti-Fyb cause HDN and HTRs and are common in endemic areas where natural selection of persons with the Fya-b- phenotype is favored due to resistance to Plasmodium vivax infection<sup>[8]</sup>.

Anti-Jka and anti-Jkb are rare and may cause delayed HTR and HDN. Anti-Yta and anti-Ytb are extremely rare and are of no clinical significance. Pregnant women with antibodies to high incidence blood group antigens should be diagnosed as early as possible. An indirect Coombs test should be obtained in all pregnant patients at their first prenatal visit, after which titers are made if found positive.

There are several *in vitro* tests that attempt to mimic fetal conditions that produce red blood cell hemolysis such as the ADCC assay, the monocyte monolayer assay and the monocyte chemiluminescence test all of which try to predict the need for intrauterine fetal blood transfusion. Percutaneous umbilical blood sampling plays a major role in treating hemolytic disease of the fetus, and is an alternative to serial spectrophotometric measurements of fetal blood specimens to identify fetuses at high risk of having antenatal anemia<sup>[9]</sup>.

## MATERIAL AND METHODS

The study involved 1195 consecutive samples from pregnant women consulting at King Khaled University Hospital, Riyadh over a period of

two years. Data were acquired by standardized methodology using forms that were completed during antenatal care. Demographic data were collected from patient files, and from our knowledge that no data was available for the incidence of HDN in this hospital. Blood samples were collected from pregnant women by trained nurses and submitted to the blood bank. All samples were centrifuged 3000 x g for five minutes and separated. Samples were either done at the same time or frozen at -2 °C and assayed later.

ABO blood grouping was done using Diaclon typing cards (DiaMed-ID, Cressier/Switzerland). All blood group tests were confirmed with the reverse serum test with known test red cells. Negative controls were included in all tests. ABO blood group tests were performed only at room temperature. Reverse group cells were supplied by Gamma Biologicals. Rh grouping was done using Diaclon anti-D monoclonal (Diamed Cressier/Switzerland). Rhesus controls were applied in all tests. When applicable, the weak D (Du) procedure was performed by adding Diaclon Rhesus control to patients' red cell suspension and incubating it for 15 min at 37 °C. After washing with isotonic saline Diamed AHG was added and immediately spun. The cells were re-suspended gently and observed macroscopically for agglutination. Negative reactions were confirmed with Diamed Coombs control cells.

Antibody screening was done using the Diamed ID Micro typing system-antibody (Cressier/Switzerland) and screened by the ID Card combined with Coomb's and enzyme test which offers complete antibody screening for one donor in an easy single step using ID Dia Cell I+II+III test cell reagents for the indirect antiglobulin test procedure and ID DiaCell I+II+III papainized test cell reagent for the enzyme technique. Human group O red cells from single donors in a buffered suspension medium at 0.8% were used during testing.

Test cell reagents were allowed to reach room temperature before use. 50ul of ID Dia Cell I+II+III and ID DiaCell I+II+IIIP were pipetted to the appropriate microtubes (1-3 and 4-6) respectively. Serum (25 ul) was added to each microtube. The cards were incubated for 15 min. at 37 °C in the ID incubator. The ID cards were centrifuged for 10 minutes in the ID centrifuge.

The interpretation for all tests done in glass tubes was performed using grades of agglutination ranging from + to +++++, whereby the result is recorded as positive, or negative when any sign of agglutination is absent. For all card tests, a positive result means agglutinated cells form a red line on the surface of the gel in the microtube or agglutinates dispersed the gel. A negative result means the presence of a compact button of cells on the bottom

**Table 1:** Distribution of blood groups among Saudi pregnant women in the study

	O	A	B	AB
Rh +	524	284	177	41
Rh + %	43.9	23.8	14.8	3.4
Rh -	70	44	44	11
Rh - %	5.9	3.7	3.7	0.9
Total	594	328	221	52
Total %	49.7	27.4	18.5	4.4

of the microtube.

Antibody titration was obtained by testing serial dilutions of a serum against selected cells from Diamed. The results were expressed as the reciprocal of the highest serum dilution that causes macroscopically apparent agglutination. Titration scores can provide information about the amount of antibody in a serum or the amount of antigen present on red cells. Titration ranged from 1:1 to 1:2048, when applicable, using the patients' serum and test cells which were incubated at 37 °C for one hour after which AHG method was done when required. The end point is reported as the reciprocal of the test tube that last shows macroscopic agglutination. Titration was performed in the following situations:

1. Prenatal studies: the mother's serum is tested at intervals during pregnancy.

2. Antibody identification: some antibodies cause universal agglutination when undiluted serum is used but comparing titration results may indicate specificity.

The ABO and Rhesus blood groups were determined, screened for alloantibodies after which, the type of alloantibodies present were determined. Alloimmunized patients' files were reviewed for the history of blood transfusion, medical history, number of pregnancies, husband's blood group, presence of alloantibodies among their children, whether the latter were given treatments such as blood transfusion and exposure to ultraviolet light and if they were diagnosed to have hemolytic disease during the neonatal period.

#### STATISTICAL METHODS:

All analysis was performed using the Instat (Instat Biostatistics, Graphpad Package USA). Normal distributed data were analyzed using student t-test and values calculated. Mann-Whitney test was also used. The two-sided p-value was applied and a value less than 0.05 was considered significant

#### RESULTS

The results of blood grouping are shown in Table 1. Type O had the highest prevalence at 594 (49.7%) out of the total, with 524 Rh (D) positive (43.9%)

**Table 2:** Distribution of red blood cell antibodies in alloimmunized pregnant subjects

Antigen System	Antibody positive cases	Percentage	Total percentage
Rh			
D	12	28.57	
C	2	4.76	
Cw			
C			52.38
E	6	14.28	
E	2	4.76	
Kell			
K	1	2.38	2.38
K	0		
Kidd			
Jka	1	2.38	2.38
Jkb	0		
Lewis			
Lea	1	2.38	2.38
Leb	0		
Duffy			
Fya	0		2.38
Fyb	1	2.38	
MNS			0
Lutheran a & b	0	0	0
Non-specific	2	4.76	4.76
Autoantibodies	14	33.33	33.33
Total	42	100	

and 70 subjects Rh (D) negative (5.9%). Blood type A was seen in only 328 (27.5%) among whom Rh (D) positive were 284 (23.8%) and Rh (D) negative were only 44 (3.7%). Blood type B subjects numbered 221 (18.5%), among whom Rh (D) positive were 177 (14.8%) and Rh(D) negative 44 (3.7%). Blood type AB subjects numbered 52 (4.4%), among whom Rh(D) positive (3.4%) and Rh(D) negative 11 (0.9%). Generally, Rh (D) positivity was present in 1026 (85.9%) of subjects against 169 (14.1%) Rh negative.

Screening for alloantibodies identified five types of alloantibodies in addition to non-specific and autoantibodies. Table 2 shows specificities of identified antibodies in immunized pregnant women. The most frequent (52.38%) were against the Rhesus system, against the Kell system, 2.38 %; against the Duffy system 2.38%; 4.76% were non-specific antibodies and 33.3% were autoantibodies.

The frequency of clinically significant alloimmunization causing hemolytic disease or hemolytic transfusion reactions were: anti-D, 12 (28.57%), anti-C, 2 (4.76%), anti-E, 6 (14.28%) and anti-e, 2 (4.76%); only one (2.38%) developed anti-K; anti-Jk, one (2.38%); one had anti-Le (2.38%); there was one (2.38%) with anti-Fy (Table 2).

In summary, 1.84 % of the total number of study subjects were alloimmunized by antigens of the Rh system while 0.08% were alloimmunized to antigens

**Table 3:** Percentage of pregnant women with alloantibodies according to the antigen systems

Antigen System	Rhesus	Kell	Kidd	Lewis	Duffy
Frequency of antibodies	22	1	1	1	1
Percentage of antibodies	1.67	0.08	0.08	0.08	0.08
Percentage of alloimmunized	1.84	0.08	0.08	0.08	0.08

**Table 5:** The incidence of alloimmunization in Rh D positive and Rh D negative women

	O		A		B		AB	
	Rh+	Rh-	Rh+	Rh-	Rh+	Rh-	Rh+	Rh-
Rh								
D		5		3		3		1
C		1		1				
Cw								
E	3		2				1	
e	1				1			
Kell								
K	1							
Kidd								
Jka	1							
Jkb								
Lewis								
Lea	1							
Leb								
Duffy								
Fya								
Fyb	1							
MNS								
Lutheran a & b								
Non-specific	1							
Auto- antibodies	10	1	2			1		
Total	19	7	4	4	2	4	1	1
	26		8		6		2	
%	45.2	16.7	9.5	9.5	4.8	9.5	2.4	2.4
	61.9		19		14.3		4.8	

either from the Kell, Kidd, Lewis or Duffy system (Table 3). The number of pregnant women negative for alloantibodies was 1171 (98%), those with only one alloantibody 22 (1.8%), while only two women had a combination of two kinds of alloantibodies (0.2%), (Table 4).

Most alloantibodies were detected in patients with blood group O - 26 (61.9%) followed by blood group A - 8 (19%), blood group B - 6 (14.3%), and blood group AB - 2 (4.8%). Anti-D antibodies were present in five women with blood group O, Rh negative; in three women with group A, Rh negative; in three women with group B Rh negative, and one with group AB, Rh negative blood. Anti-C antibodies were present in one woman who was group O, Rh negative and in one woman with group A, Rh negative blood. Anti-E antibodies were present in three women with group O Rh positive blood, and also in two women

**Table 4:** Number of pregnant women in relation to alloantibodies

No. of pregnant women	Percentage	No. of alloantibodies developed
1171	98	0
22	1.8	1
2	0.2	2

with group A Rh positive blood. Only one AB, Rh positive woman showed anti-E antibodies. Anti-e antibodies were present in one woman with group O, Rh positive blood and in one woman with group B, Rh positive blood. There was only one incident of anti-K antibodies in one patient with group O, Rh positive blood. There was one incident each of anti-Jk anti-Le and, anti-Fy, all of whom had group O, Rh positive blood. Non-specific antibodies were detected in one patient with group O, Rh positive blood and in one for group B, Rh positive blood. Lastly, autoantibodies were present in 10 women with group O, Rh positive blood, in one with group O, Rh negative blood, in two with group A, Rh positive blood and in one with group B, Rh negative blood (Table 5). 1.8% were blood group A, four (2.4%) were blood group B and one (0.6%) had blood group AB blood.

The files of women in whom alloimmunization was detected were reviewed for history of previous pregnancies, transfusions, abortions, dilatation and curettage procedures or cesarean section (Table 6). Demographically old, most of the subjects' age ranged from 24 to 43 years. Most of the detected alloantibodies were of low titer. Ten of alloantibodies identified in the alloimmunized pregnant women were weak in titer- 4 with titer 2, 2 with titer 4, 2 with titer 8, one with titer 16, 2 with titer 32 and 2 with titer 256. Alloantibodies were present in seven live-born infants. Five of these needed treatment. One infant needed phototherapy only, while two needed a combination of ultraviolet phototherapy and blood transfusion. One needed to be admitted to the neonatal intensive care unit (NICU) while the last one received blood transfusion. In addition there were two infants who needed exchange transfusion due to hyperbilirubinemia but no antibodies were detected (Coomb's test negative).

All the alloimmunized Rh negative patients with anti-D had husbands who were Rh positive and gave children with positive Rhesus blood groups. One of the alloimmunized patients had a previous history of anti-D immunization, one had six previous pregnancies and the others had no known history of exposure to antigens. One woman with anti-D alloantibodies gave birth to seven babies with the following consequences: five needed treatment, one needed phototherapy, two

**Table 6:** The clinical data of pregnant women who were alloimmunization positive and their husband and baby

Clinical data of pregnant women who were alloimmunization positive							Husband		Baby			Treatment
No	Age	ABO	Rh	Ab type	Ab titer	Previous history	ABO	Rh	ABO	Rh	Ab Detection	
1	30	O	+	anti-K	1:2	Grav. 5, para 3+0	B	+	O	+	NO	NO
2	31	O	+	anti Jka	1:1	unknown	A	+	A	+	NO	NO
3	40	O	+	anti E	1:1	P6+ve	O	+	O	+	NO	bilirubin high, BT
4	30	O	-	anti D	1:16	known case Rh	B	+	B	+	YES	UV
5	42	O	-	anti D	1:4	six gravida	A	+	A	+	YES	NO
6	38	O	+	anti E	weak	two abortions	O	+	O	+	NO	NO
7	38	A	-	anti D	1:32	unknown	A	+	A	+	YES	UV & BT
8	32	B	+	anti e	weak	two gravida, hemorrhage	O	+	O	+	NO	NO
9	18	O	-	anti D	weak	unknown	B	+	B	+	NO	NO
10	43	A	+	anti E	Weak	P6+ve	O	+	O	+	NO	BT
11	41	O	-	anti D	1:32	unknown	A	+	A	+	YES	BT
12	25	O	+	anti Lea	weak	unknown	A	+	O	+	NO	NO
13	30	A	+	anti E	1:4	blood transfusion	O	+	O	+	NO	BT
14	28	O	+	anti E	1:1	blood transfusion	O	+	O	+	NO	BT
15	40	AB	-	anti D	1:8	cesarean,	A	+	A	+	YES	NICU
16	39	O	-	anti C+D	1:16	cesarean, diabetes mellitus	O	+	O	+	NO	NO
17	37	B	-	anti D	1:8	diabetes, RA	O	+	O	+	YES	NO
18	24	A	-	anti D	1:1	abortion, rubella+ve	A	+	A	+	NO	NO
19	39	AB	+	anti E	weak	5 gravida	O	+	O	+	NO	NO
20	33	O	+	anti Fyb	weak	cesarean, abortion	O	+	O	+	NO	NO
21	31	B	-	anti D	1.256	recurrent fetal loss	O	+	-	+	-	-
22	31	B	-	anti D	1.256	unknown	B	+	B	+	YES	bilirubin high, BT
23	24	A	-	anti C+D	weak	unknown	O	+	O	+	NO	NO
24	33	O	+	anti e	weak	unknown	O	+	O	+	NO	NO

Ab: antibodies, UV: ultraviolet treatment, BT: blood transfusion, RA: rheumatoid arthritis  
The remaining women, not included in this table were normal

were given phototherapy and blood transfusion, one had to be admitted to NICU and the last one received blood transfusion. Two women with anti-C antibodies were shown to have concurrent anti-D antibodies (anti- C + D) but these antibodies were not detected in their respective neonates. Six cases with anti-E antibodies had titers which ranged from weak up to 4. Two of them had a previous history of G6PD deficiency, one had a history of two abortions and two had a history of blood transfusion. None of the alloimmunized patients gave birth to neonates who were positive for anti-E antibodies. Two babies were given blood exchange transfusion due to hyperbilirubinemia but no antibodies were detected. Two patients with anti-e antibodies gave weak reactions. One patient had two previous pregnancies and an episode of puerperal hemorrhage, while the others had unknown history of immunization (Table 6). Respective neonates of these mothers also gave no reaction indicative of alloimmunization.

There was one case with an anti-Kell titer of 2, who had five previous pregnancies but no antibody was detected in all of them. There was one case of anti Jk with a titer of 2 but no identifiable alloantibodies were found in the offspring. There was one case with anti-Le antibodies with weak titer; offspring

was negative for any alloantibodies. One patient with anti-Fy antibodies (with weak reaction) had a previous cesarean section, transfusion and abortion but alloantibodies were not detected in the newborn.

## DISCUSSION

The study of blood groups of women in the Riyadh region indicated that the highest blood group is O (49.71%), followed by A (27.45%), B (18.49%) and AB (4.35%). The high frequency of O blood group is not unique in women in the Riyadh region as similar findings were seen in Tabuk, Madina Munawwara and Eastern Province which indicates that blood group O is not related to the Riyadh region but that it is most likely common to Saudi Arabia.

The blood groups in the Tabuk area were (53.02%) for O, (30.12%) for A, (12.04%) for B and (4.02%) for group AB while the blood groups in Madina Munawwara were group O (44.8%), group A (28.9%) group B (20.7%) and (5.5%) for group AB<sup>[10]</sup>. Blood group distribution of women in the Eastern province showed group O, 45.3%, group A 27.3%, group B, 20.8% and 6.6% for group AB<sup>[11]</sup>. Therefore the chance of ABO incompatibility



occurring among the offspring of mothers of the O blood group should be taken into consideration more often if the father's blood group is not O.

In contrast blood group O and B are more frequent in women of Arabic speaking populations in Turkey. Blood group A is reported to be highest (49%) in Turkish women<sup>[12]</sup>.

In the Central Province Rh positivity was 85.86% against 14.14% Rh negative, while Rh negatives in the Eastern province reached only 1.9%<sup>[11]</sup>; Rh negative in Madina Munawwara and Tabuk was 11 and 8% respectively<sup>[10]</sup>. This study supports the finding that the highest prevalence of Rh negative women is in the Riyadh region. Prevalence of this group in England is 17% and 14.7% in Turkey. In Sweden approximately 17% of all mothers were Rh D negative - this implies an immunization frequency of 1.1% in this population<sup>[13]</sup>.

The Rh blood group comprises more than 40 individual antigens of which five are routinely identified: DCcE and e. The first Rh antigens discovered were the D+ and the D- phenotypes. Because of the light linkage between the D and C/cE/e loci however these five antigens are inherited. Certain genotypes are more common than others although gene frequencies vary from one population to another. The frequency of Rh negativity is lower in Saudi Arabia suggesting prevalence of more African blood group markers<sup>[14]</sup>.

During birth, blood cells from the fetus can escape into the mother's bloodstream. These cells are recognized as foreign if they are a different blood type from the mother and a natural rejection process will ensue with the formation of antibodies. The process is known as red blood cell alloimmunization. This event typically occurs after the delivery of a baby at the end of pregnancy but other pregnancy related events such as abortion can result in antibody formation. The British Committee for Standards in Hematology and Blood Transfusion Task Force (Chairman P. Kelsey, 2003)<sup>[15]</sup> reported that intrauterine transfusion in the alloimmunized women increased the incidence of additional alloantibodies.

Most (98%) of the Saudi pregnant women who participated in this study showed no antibodies, *i.e.*, they were non-immunized. Most of the immunized women (n = 22, 1.8%) developed only one type of alloantibodies, while 0.2% developed two types of antibodies.

The study shows that immunization due to antibodies belonging to the Rhesus system is about 1.84% of all examined Saudi pregnant women. The Anti-D group formed 28.57% of the alloimmunized cases. Despite the use of rhesus immunoglobulin anti-D is still a common antibody identified. Moncharmont *et al*<sup>[5]</sup> reported that the percentages

of HDN with anti-D alloimmunization was 98.4, 93.5 and 68.1% respectively. Holtzman *et al*<sup>[11]</sup> demonstrated that anti-D accounts for less than 20% of all identified red blood cell antibodies. Vietor *et al*<sup>[16]</sup> found that women with anti-D were generally considered to have high responses in producing red blood cell antibodies outside the Rh system. Ten percent of women with pre-existing anti-D had more than one alloantibody other than Rh system antibodies. Mayne *et al*<sup>[17]</sup> reported that the gene for the partial D or Du is Ce-linked in most families and only rarely with cE or ce.

Anti-C antibody was found in about 4.76% of the immunized patients. Baker *et al*<sup>[18]</sup> reported one case on a group A Rh positive, C negative woman in whom anti-C was developed as a result of blood transfusion in childhood.

Hardy and Napier<sup>[19]</sup> in their review of red blood cell antibodies among Rh positive women in South and Mid-Wales over a 30 - year period, described two infants with hemolytic disease caused by anti-C who died, one after an exchange transfusion and one without undergoing exchange transfusion.

Bowman *et al*<sup>[20]</sup> mentioned that the prevalence of anti-C and anti-Ce alloimmunization ranged from 8.7 to 185 / 100,000 pregnancies. The incidence of affected babies requiring treatment compared with the total number of anti-C and anti-Ce alloimmunized pregnancies ranged from 2.6 to 22.2%.

No anti-Cw or anti-c was detected in the current study. Anti-Cw is a rare antigen occurring in about 2% of the white population. The specific antibody, anti-Cw either occurs together with anti-C or more rarely alone like most Rh antibodies. Anti-Cw can cause hemolytic transfusion reactions and HDN. But anti-c is one of many atypical antibodies that can be produced by Rhesus D positive patients during pregnancy. Maternal anti-c alloimmunization appears to be a rare cause of fetal death. However multiple transfusions on different occasions or transfusion plus pregnancy may contribute to the development of clinically apparent c-hemolytic disease. The great proportion of previously transfused mothers may partly account for the greater number of cases of severe c-hemolytic disease. Furthermore, the titer of maternal antibody correlated poorly with severity of hemolytic disease except that very low titers were not associated with either moderate or severe disease according to Denomme *et al*<sup>[21]</sup>.

In this study, the anti-E and anti-e were found to be 14.28 and 4.76% respectively among Saudi immunized pregnant women. Vietor *et al*<sup>[16]</sup> reported only one case who developed anti-E antibodies.

In summary, the number of antibodies against antigen of the rhesus system formed the highest

percentage (52.38%) of the alloantibodies detected.

The Kell system antibodies were found only in one pregnant woman forming 2.2% of the total antibodies detected in the study group. HDN due to anti-k alloimmunization of the mother is very rare. Monchamont *et al*<sup>51</sup> collected 3000 cases of HDN over thirty years. Among these 273 (9.1%) were due to alloantibody other than anti-D and only three cases of anti-k HDN (1.09%) were found; two of them required exchange transfusion after delivery. Bowman *et al*<sup>221</sup> reported 3426 cases of alloimmunization in about 175,000 women and found only one due to anti-k (0.03%). While in 1992<sup>201</sup>, he explained that the rarity of severe Kell hemolytic disease is almost entirely due to the rarity of any degree of Kell hemolytic disease. When antibody screening of Rh positive pregnant women was universal, only eight of 324 (2.5%) Kell – immunized pregnancies ended in delivery of affected infants during the twenty year study period.

Kell hemolytic disease is rare because Kell immunization is usually produced by blood transfusion. In addition only 9% husbands of the women studied were Kell-positive out of whom 98% are heterozygous for Kell. It is observed that when Kell hemolytic disease occurs it can be as severe as Rh (D) hemolytic disease. Wenk *et al*<sup>22</sup> reported that Kell antibodies were encountered in reproductive women about 60% as often as Rh o antibodies but the risk of Kell disease is less than 5% when such antibodies are detected. Holtzman *et al*<sup>11</sup> studied 121 cases (22%) of Kell alloimmunization. This frequency is even higher than that of D alloimmunization (101, 18.4%).

Immunization against the Kidd system is also very rare. We detected only one anti-Jka case (2.38%) among the immunized Saudi pregnant women. Viotor *et al*<sup>161</sup> reported one case of anti Fya as a result of intrauterine transfusion. Center for Disease Control<sup>231</sup> reported a case complicated by the presence of anti-Fyb with a titer of 32 due to blood transfusion.

In this study, the percentage of Lewis system was 2.38% of the alloimmunized Saudi pregnant women in the form of anti-Lea. Lewis antibodies are the commonest single cause of positive results in pre-transfusion antibody screening tests. They occur without obvious stimulation by transfusion or pregnancies and so can be found the first time a serum is tested. Occasionally anti-Lea but not anti-Leb can cause severe transfusion reactions with hemoglobinemia and hemoglobinuria. Lewis antibodies do not cause HDN because they are almost always IgM and because newborn infants group as Le a – b –.

This study indicates that the percentage of alloimmunization among Saudi pregnant women

is low. Alloimmunization to the Rhesus system was 1.84% in the study population. This low incidence is mostly due to the early detection of Rh negativity of the mothers before or as early as possible during pregnancy. Also, giving D-immune globulin after delivery for the Rh negative mothers lowered alloimmunization rates. In the United States, with the widespread use of D-immune globulin, it was once thought that Rh alloimmunization in pregnancy could be eradicated. The rate of HDN due to Rh antibody declined from 45.1 cases/10,000 total births in 1970 to a rate of 15.6 cases/10,000 total 1983, (Center for Disease Control, 1985)<sup>231</sup>. Though not entirely eradicated, Rh alloimmunization has dropped markedly due to immune globulin administration and improved transfusion practices.

We detected most cases of alloimmunization in blood group O (61.9%) women, followed by group A (19%) then group B (14.3%) and lastly group AB with 4.8% of all immunized pregnant women. Alloimmunization in Rh (D) negative women was 8.3%. The incidence of Rh alloimmunization could be reduced to 0.18% if a single dose of Rh immune globulin was administered at 28 weeks gestation. Also they proposed that the routine use of antenatal RhIg in Rh negative women would be 88% effective in preventing sensitization.

All immunized mothers with anti-D in the serum were rhesus negative and their husbands were Rh positive and gave birth to babies who were rhesus positive. The titer of anti-D ranged from weak to high. One alloimmunized patient had a previous history of anti-D immunization; one gave six live births, another had a history of recurrent fetal loss possibly due to alloimmunization with anti-D and the rest had unknown history of immunization with anti-D. There were two cases of anti-C linked with anti-D but was not detected in the neonate.

In six cases of anti-E the titer ranged from weak up to 4. Two of the anti-E cases have a previous history of G6PD deficiency, one has a previous history of two abortions, and two have a history of blood transfusion and the last one had unknown history of immunization. Two babies given blood exchange due to hyperbilirubinemia may have been due to G6PD deficiency because no antibodies were detected.

The two patients with anti-e gave weak reactions. One patient gave history of live births and puerperal hemorrhage and the other had unknown history of immunization. Neonatal blood examinations gave no indication of alloimmunization.

There was one case of anti-kell with a titer of 2. She had five live births but the antibody was not detected in the most recent offspring. There was only one case of anti-Jka with a titer of 1. The baby

of the immunized patient gave no evidence of alloantibody in his blood. Anti-Le was detected in one patient with weak titer and gave no reaction in the newborn. There was only one case with detected anti-Fyb but the reaction was weak. The mother had previous cesarean section, transfusion and one abortion. The alloantibody was not detected in the newborn.

### CONCLUSION

Even if Rh D alloimmunization is still a dominant problem giving rise to hemolytic disease and transfusion reactions, the relative importance of antigens other than Rh D have increased since the introduction of Rh D prophylactic treatment. Alloimmunization to E, c and Kell antigens can reach significant proportions of studied populations and can result in deleterious effects on the fetus. Forty-six percent (46%) of alloimmunization cases and 22% of exchange transfusions were in patients with antibodies to these three antigens.

The actual risk of alloantibody production during pregnancy is unknown but stimuli for antibody production are fetomaternal bleeds that occur throughout pregnancy but occur most frequently at the time of delivery.

Screening for irregular antibodies during pretransfusion reduce the sensitization of red blood cells and reduce the risk of occurrence of hemolytic disease due to antibodies other than to the Rh group of antigens.

Blood to be transfused to women planning future pregnancies should be compatible not only with the D antigen status of the patient but also with her Kell and other Rh antigen status.

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## Original Article

# The Effect of Ramadan Fasting on Surgical Emergency Attendants

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**ABSTRACT**

**Objectives:** To study the effect of Muslim fasting on health in general, during Ramadan, Shabaan and Shawaal

**Design:** Retrospective cohort study

**Setting:** Surgical Department, Al-Sabah Hospital, Kuwait

**Subjects:** All patients (n = 61,832) who attended the Surgical Department during three consecutive lunar months each year (the fasting month - Ramadan, the month before - Shabaan and the month after - Shawaal), for the last five consecutive years were included. 85% were Muslims (Mixed Group). The study was further refined to analyze Kuwaiti patients who were all Muslims (Muslim Group).

**Main Outcome Measure:** Attendance at the Surgical Department

**Results:** Attendance in the Mixed Group was less during

Ramadan and Shawaal in comparison to the attendance during Shabaan (p = 0.06). In the Mixed Group, attendance during Shawaal was much less than Shabaan (p = 0.0007). Patients in the Muslim Group attending the Surgical Department (2000 – 2004), showed a decrease in attendance during Ramadan and Shawaal in comparison to Shabaan (p = 0.015). The total number of cases admitted to the hospital through the Surgical Department was less in Ramadan and Shawaal in comparison to Shabaan (p = 0.6).

**Conclusion:** There is a decrease in the number of Muslim patients attending Surgical department during the fasting month of Ramadan and Shawaal in comparison to Shaaban. This may indicate that Muslim fasting may have a positive effect on decreasing the number of patients attending the Surgical Department.

KEY WORDS: emergency, fasting, Muslims, Ramadan, surgery

**INTRODUCTION**

Ramadan is the ninth lunar month in which Muslims believe that the Holy Book "The Qur'an" was sent to Prophet Mohammed (PBUH). More than 600 million adult Muslims worldwide practice fasting during this month, as stated in The Qur'an, from dawn to sunset. Children and sick individuals are exempted from this fasting. Muslims fast to express their gratitude to God and they believe that fasting improves health. There are many centers worldwide who advise fasting, not on religious basis, but for improving health<sup>[1]</sup>.

In this study we tried to demonstrate the possible beneficial effect of fasting on health by studying the attendance of patients at the Surgical department for five consecutive years.

**PATIENTS AND METHODS**

In a retrospective analysis, we studied patients who were treated in the Surgical Department in Al-Sabah Hospital, Kuwait during three consecutive lunar months, the fasting month (Ramadan),

the month before (Shabaan) and the month after (Shawaal), for five consecutive years (2000-2004). Our study included 61,832 patients of whom a majority (85%) was Muslim (Mixed Group). Then the study was refined to analyze Kuwaiti patients who are all Muslims (Muslims Group).

The number of patient visits to the Surgical Department in Ramadan, the month before and the month after (30 days each) were analyzed. Our aim was to see if there is any difference in the number of patient attendance during these three months and to demonstrate the positive or negative impact of fasting on health in general.

**Statistical methodology:**

Data were collected and coded then entered into an IBM compatible computer using the SPSS version 12 for Windows. Entered data were checked for accuracy and normality using Kolmogorov-Smirnov and Shapiro-Wilk tests and proved to be normally distributed. Qualitative variables were expressed as number and percentage while

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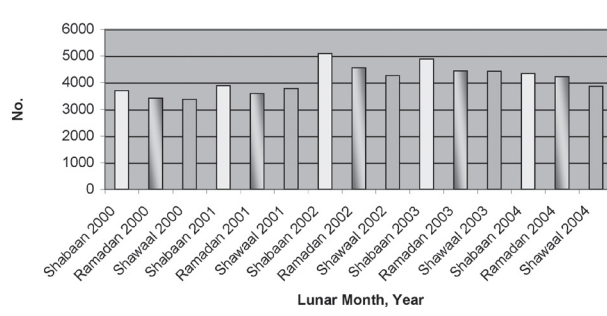


Fig. 1: Surgical Unit cases (Mixed group) attendance during Shabaan, Ramadan and Shawaal (2000 - 2004, p value = 0.06)

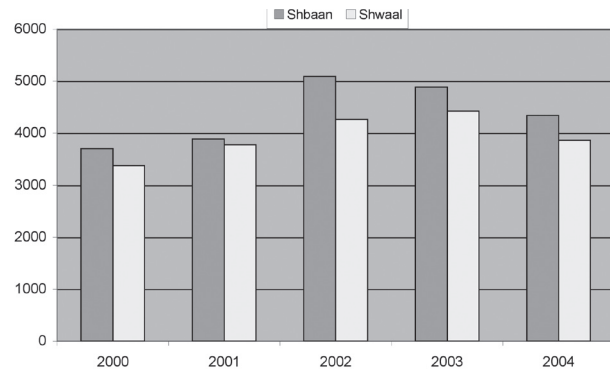


Fig. 2: Surgical Unit cases (Mixed Group) attending during Shabaan and Shawaal (2000-2004, p value = 0.0007)

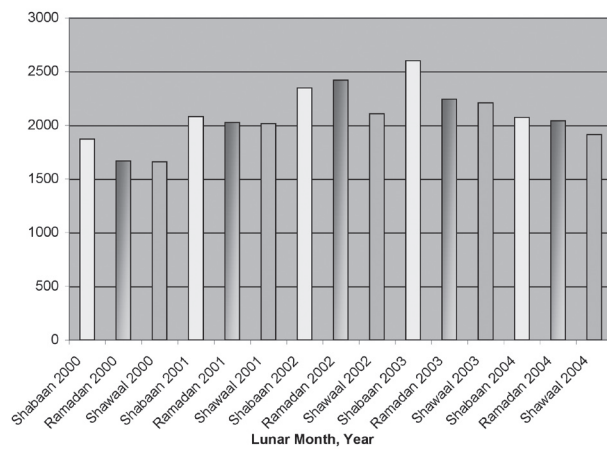


Fig. 3: Surgical Unit cases (Muslims Group) attending during Shabaan, Ramadan and Shawaal (2000-2004, p value = 0.015)

– 2004), showed a statistically significant decrease in the number of cases attending during Ramadan (10,396 patients) and Shawaal (9,902 patients) in comparison to those attending during Shabaan (10,968 patients,  $p = 0.015$ , Fig. 3).

DISCUSSION

The aim of this study was to evaluate the relationship between Ramadan fasting and health in general by studying the number of the patients attending the Surgical Department in our hospital for five consecutive years during Ramadan, Shabaan and Shawaal months.

Many research workers studied the effect of fasting practiced by Muslims during Ramadan on human health in normal individuals and in patients suffering from diseases like diabetes mellitus, hypertension, heart diseases, stroke incidence, peptic ulcer disease as well as pregnancy with biochemical and hematological changes.

Two studies were found in the literature which showed some negative effect of Ramadan fasting on human beings. The first was by Langford *et al* who found some increase in the number of attendants to surgical casualty in Ramadan (limited study)<sup>[2]</sup>. The second was by Donderici *et al.* who found that fasting in Ramadan increases peptic ulcer complications in patients suffering from peptic ulcers<sup>[3]</sup>.

The majority of the studies found no negative effect of Ramadan fasting on healthy individuals or on patients, although some found significant metabolic changes with different diseases, *e.g.*, diabetes or hypertension<sup>[4-16]</sup>.

In our study, we compared the fasting month (Ramadan) with Shabaan and Shawaal months for five consecutive years trying to eliminate the factors that could affect the number of patients attending the Surgical Department such as the environment, temperature and vacations.

Our study involved 61,832 patients who attended the Surgical Department during this period. We found a statistically significant decrease in the number of cases attending Surgical Department

quantitative variables were expressed as mean and standard deviation. The arithmetic mean was used as a measure of central tendency, while the standard deviation was used as a measure of dispersion. The one way ANOVA (F-test) was used as a parametric test of significance for comparison between more than two sample means, using either Scheffe's or Tamhane's post hoc tests for paired comparison according to the results of homogeneity testing. A 5% level was chosen as a level of significance in all statistical significance tests used.

RESULTS

The number of patients in the Mixed Group (85% were Muslims) attending the Surgical Department during Ramadan (20,226 patients) and Shawaal (19,702 patients) was less during each of these two months in comparison to number of those attending during Shabaan (21,904 patients,  $p = 0.06$ , Fig.1).

By comparing the number of cases (Mixed Group) attending Surgical department during Shawaal and Shabaan, we found a statistically significant decrease in the attendance during Shawaal ( $p = 0.0007$ , Fig. 2).

Analysis of the number of patients in the Muslims Group attending the Surgical Department during Shabaan, Ramadan and Shawaal (2000

during the fasting month (Ramadan) and Shawaal month compared to the Shabaan month, especially in the Muslims Group.

We also found a significant decrease in the number of patients attending during the Shawaal month in comparison to the Shabaan month in both groups (Mixed and Muslim). This may indicate that there is a possible effect of fasting that may extend to months after Ramadan.

### CONCLUSION

There is a decrease in the number of Muslim patients attending the Surgical Department during the fasting month of Ramadan and Shawaal in comparison to the Shaaban month. This indicates that fasting may have a positive effect on decreasing the number of patients coming to the Surgical Department.

### ACKNOWLEDGEMENT

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## Original Article

# Is Brucellosis a Common Infectious Cause of Pyrexia of Unknown Origin in Kuwait?

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Kuwait Medical Journal 2008, 40 (2): 127-129

## ABSTRACT

**Objectives:** To investigate the prevalence of brucellosis and to compare it with other causes of pyrexia of unknown origin (PUO) in Kuwait

**Design:** Retrospective study

**Setting:** Infectious Disease Hospital, Kuwait

**Subjects:** All patients admitted to Infectious Disease Hospital with a diagnosis of PUO between January 2001 and December 2004 were included in this study.

**Main Outcome Measures:** Age, gender, nationality, occupation, residence and laboratory investigations

**Results:** One hundred thirty six patients were admitted with PUO to the hospital. Their mean age was 36.7 ± 11.69 years (range: 14-80 years). The mean duration of hospitalization was 8.7 ± 7.8 days. Infectious diseases were the most common causes of PUO. Brucellosis was diagnosed in 80 (58.8%) patients, respiratory tract infection

in 10 (7.4%), gastrointestinal diseases in 14 (10.3%) and HIV was diagnosed in three patients. Other diseases such as thyroiditis and glaucomatous hepatitis were diagnosed in 15 (11%) patients. Brucellosis patients had high alanine amino transferase (ALT) level and lower white blood cell (WBC) count than other PUO patients (56.9 ± 40.6 Vs. 38 ± 31.4,  $p < 0.003$  and 7.1 ± 3.9 Vs. 8.5 ± 4.04,  $p < 0.01$  respectively). Brucellosis was common among Asian population (58.8% compared to Gulf residents 31.3% and other nationals 10%,  $p = 0.022$ ). Brucellosis is common among patients in high-risk occupations (62.5% compared to non-high risk occupations 37.5%,  $p < 0.0001$ ).

**Conclusion:** Brucellosis is the common infectious cause of PUO among Asian and patients in high-risk occupations in Kuwait.

KEY WORDS: KEY WORDS: brucellosis, Kuwait, pyrexia of unknown origin

## INTRODUCTION

Brucellosis remains a major public health problem in many developing countries<sup>[1-3]</sup>. Transmission of *Brucella* can be the result of oral ingestion, direct contact *via* skin abrasion and mucous membranes (including the conjunctiva), and inhalations. Risk factors for infection include handling of infected animals, ingestion of contaminated animal products such as unpasteurized milk and milk products (including cow, goat, and camel milk), meat, and handling of specimen cultures. Diagnosis of human brucellosis relies on blood culture and serological tests, including the standard tube agglutination test (STAT), Coombs test, and enzyme-linked immunosorbent assay (ELISA)<sup>[4,5]</sup>. Data from developing countries in the Mediterranean basin, particularly the Middle East, report seroprevalence rates ranging from 8% in Jordan to 12% in Lebanon and Kuwait<sup>[6,7]</sup>.

Back pain, headache, fever, chills, night sweats, weakness, myalgia, arthralgia, bone pain are

common presenting features. Brucellosis as a cause of pyrexia of unknown origin was not intensively highlighted<sup>[8]</sup>. The objective of this study was to investigate prevalence of brucellosis and to compare it with other causes in patients with pyrexia of unknown origin (PUO) in Kuwait.

## SUBJECTS AND METHODS

Between January 2001 and December 2004 all patients who were admitted to Infectious Disease Hospital (IDH) with PUO were included in this study. Patient's records were reviewed for age, gender, nationality, occupation and residence. Laboratory investigations such as IgA, IgG, IgM for brucella and blood culture were recorded. Blood cultures were done automatically.

PUO is defined as body temperature higher than 38.3 °C on several occasions and lasting longer than three weeks, with the etiology remaining uncertain after one week of investigation.

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**Table 1:** Demographic characteristic of the patients

	Brucellosis n (%)	Other PUO n (%)	Total n (%)	p-value
Age (in years)	36.7	31.4	34.5	0.035
Gender				
M	71 (88.8)	46 (82.1)	117 (86.0)	0.274
F	9 (11.3)	10 (17.9)	19 (14.0)	
Nationality				
GCC	25 (31.3)	30 (53.6)	55 (40.4)	0.022
Asian	47 (58.8)	20 (35.7)	67 (49.3)	
Others	8 (10.0)	6 (10.7)	14 (10.3)	
Occupation				
Population at exposure risk	50 (62.5)	6 (10.7)	56 (41.2)	0.001
Population not at risk	30 (37.5)	50 (89.3)	80 (58.8)	
Area				
Hawalli	10 (12.5)	18 (32.1)	28 (20.6)	> 0.05
Capital	4 (5.0)	10 (17.9)	14 (10.3)	
Jahra	21 (26.3)	3 (5.4)	24 (17.6)	
Farwania	32 (40.0)	19 (33.9)	51 (37.5)	
Ahmadi	6 (7.5)	6 (10.7)	12 (8.8)	
Mubarak	7 (8.8)	0 (0)	7 (5.1)	
Total	80 (100.0)	56 (100.0)	136 (100.0)	

**Table 3:** Serological markers and blood cultures

Test	Positive n (%)	Negative n (%)	p-value
IgA	11 (13.8)	69 (86.3)	0.003
IgG	08 (10.0)	72 (90.0)	0.021
IgM	09 (11.3)	71 (88.8)	0.01
Blood culture	67 (83.8)	13 (16.30)	0.0001

One hundred thirty six patients meeting the classic criteria of PUO hospitalized at the IDH were included in the study.

A questionnaire guide was designed specifically for this study to gather information from medical records of all patients with PUO discharged from the IDH during the period under study. Main outcome measure was the final diagnosis established at discharge. The main research variables were age, gender, nationality, occupation, residence and laboratory investigations such as IgA, IgG, IgM for brucella and blood culture.

**Statistical analysis:** Data were analyzed using SPSS version 12 for Windows. Qualitative variables were expressed as number and percentage while quantitative variables were expressed as mean and standard deviation (SD). Chi-square test was used to compare two qualitative variables. Fisher's exact test was used to compare the difference between two qualitative variables. A p value of < 0.05 was considered as statistically significant.

## RESULTS

Demographic characteristic of the patients are shown in Table 1. The mean age of the infected

**Table 2:** Final diagnosis of PUO

Diagnosis	Frequency	%
Brucellosis	80	58.8
Respiratory Symptom	10	7.4
Gastrointestinal	14	10.3
DAMA or undiagnosed	14	10.3
HIV	3	2.2
Others	15	11
Total	136	100.0

DAMA: discharged against medical advice

**Table 4:** Abnormal laboratory parameters

Parameters	Brucellosis	Other PUO	p-value
ALT (mean ± SD)	56.9 ± 40.6	38.0 ± 31.4	0.003
AST(mean ± SD)	70.9 ± 50.12	37.5 ± 26.8	0.021
WBC(mean ± SD)	07.1 ± 3.9	08.5 ± 4.0	0.01
ESR(mean ± SD)	30.8 ± 25.19	42.4 ± 33.2	0.0001

patients was  $36.7 \pm 11.69$  years (range: 14-80 years). Males were more commonly affected than females and out of them 71 (88.8%) were found to have brucellosis. More than 50% of patients who developed brucellosis were at exposure risk. A significantly higher proportion of brucellosis cases were patients from Asian countries as compared to PUO patients from other regions (58.8% Vs 35.7%,  $p=0.022$ ).

The final diagnosis of PUO is shown in Table 2. Infectious diseases were the most common causes of PUO. Brucellosis was diagnosed in 80 (58.8%) patients, respiratory tract infection in 10 (7.4%) patients, gastrointestinal diseases in 14 (10.3%) and HIV was diagnosed in three patients. Other diseases such as thyroiditis and glaucomatous hepatitis were diagnosed in 15 (11%) patients. Serological markers are shown in Table 3.

The overall seroprevalence for brucellosis based on ELISA IgG (OD > 0.6), IgM (OD ≥ 0.6) and IgA (OD ≥ 0.3) was 10, 11.3 and 13.8%, respectively. In 67 (83.8%) patients the blood cultures were positive for brucellosis. Twenty eight patients had positive serological markers as well as positive blood cultures (Table 3). Data related biochemical abnormalities are shown in Table 4. Alanine Amino Transferase (ALT) was significantly higher in brucellosis cases than other PUO patients ( $p = 0.003$ ). However WBC count was higher in other patients with PUO than brucellosis patients ( $8.5 \pm 4.04$  Vs  $7.1 \pm 3.91$ ,  $p = 0.01$ ). The most common laboratory abnormality was an elevated erythrocyte sedimentation rate (ESR) (89.6%). The mean duration of hospitalization was  $8.7 \pm 7.8$  days.



## DISCUSSION

Clinical finding, isolation from the blood and serological tests are valuable diagnostic tools for brucellosis. Isolation of *Brucella* is diagnostic of brucellosis; however in practice it is difficult due to the early tissue localization and the exacting culture requirements of the organism. In practice, blood cultures are positive in 10-30% of brucellosis cases<sup>[9]</sup> and the remainder are diagnosed serologically. There is no single test which is confirmatory for brucellosis; our data however, showed more than 80% positive for blood culture. Probably the yield of cultures improved due to better culture techniques. In the presence of appropriate signs and symptoms, a presumptive diagnosis of brucellosis is usually defined serologically as a standard tube agglutination titer of 1:160 or greater<sup>[5,9-11]</sup>. In our study IgA, IgG and IgM were positive in 11 (13.8%), 8 (10%) and 9 (11.3%) patients respectively. Investigators from the middle east have found that seroprevalence of brucellosis increases with age<sup>[5-7]</sup> and among persons with a high-risk occupation<sup>[12]</sup>.

Brucellosis is quite common in Kuwait<sup>[13,14]</sup>. *Brucellosis* was the commonest cause of PUO (59%) in our study. Male patients were affected more than females. Notably more than 50% of the infected cases from Asian and GCC population in our study were at an exposure risk. Asians were affected with brucellosis in about 60% of the cases. The clinical pattern of 400 cases of brucellosis in Kuwait was presented in 1987<sup>[14]</sup>. The disease was acute in 77%, sub-acute in 12.5% and chronic in 10.5% of cases. Raw milk was the major source of infection. The major features on presentation, irrespective of the course of the disease, were fever, sweating, headache, rigors, arthralgia, myalgia, and low back pain.

In accordance with other studies<sup>[8,15]</sup>, the present study demonstrates clearly that males are commonly affected by brucellosis. Few reports, however, have shown a higher incidence of brucellosis in females<sup>[16]</sup>. Probably this discrepancy is related to cultural and epidemiological factors. In developing countries females are in contact with domestic animals. Furthermore un-pasteurized milk and its products are widely consumed by such population. Socio-economic status of the population at risk is another important factor that might increase the risk of brucellosis. Large families are usually gathered in the same house and often sheep, goats and other domestic animals are at short distance which increases the risk of infection. Such populations are also of low educational level and history of exposure is difficult to extract from them. Therefore laboratory investigations are vital to reach to proper diagnosis.

## CONCLUSION

Infections remain the most important cause of PUO in Kuwait. Brucellosis is the common infectious cause of PUO among Asians and patients in high-risk occupations in Kuwait. Health education programs should be emphasized among high risk occupations.

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## Original Article

# The Relation between Conservative Treatment and Heel Pain Duration in Plantar Fasciitis

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## ABSTRACT

**Objective:** To establish the efficacy of conservative treatment and period of heel pain duration in plantar fasciitis

**Design:** Prospective therapeutic trial

**Setting:** Outpatient clinics at King Hussein Medical center and Prince Rashed Military Hospital, Jordan

**Subjects:** Seventy five patients with 84 heel pains were seen by a rheumatologist at the rheumatology clinic.

**Intervention:** Three arm trial therapies (only one steroid injection, heel pad, stretches and strengthening exercise).

**Main Outcome Measures:** Reduction of heel pain after

one, three and six month intervals using a 10 cm visual analogue scale (VAS).

**Results:** A marked reduction of pain score was noticed at one month in both groups. But after interviewing the patients during the clinical visits at three and six months there was a more significant improvement in pain score in the first group less than eight weeks duration in comparison with the second group

**Conclusion:** The present study demonstrates that early diagnosis and treatment could prevent long standing heel pain in plantar fasciitis.

KEY WORDS: calcaneal spur, heel pad, heel pain, plantar fasciitis, steroid, tendonosis

## INTRODUCTION

Painful heel is commonly seen in rheumatology and podiatry clinic. It has been estimated to affect 10% of runners and is present in the general population at the same rate<sup>[1-4]</sup>. It is an overuse injury resulting from repetitive micro tears of the plantar fascia at its origin on the calcaneus<sup>[2, 5]</sup>. The underlying causes may be either inflammatory or biomechanical. Some patients experience point tenderness along the medial fascia, inability to run and painful first step in the morning<sup>[3,6,7]</sup>. Recent study demonstrates absence of inflammatory cell in the injured tissue suggesting more of a degenerative process advocating the use of the terms tendonosis or fasciosis<sup>[2]</sup>.

Biomechanical factors such as pes planus, pes cavus with rigid high arch and poor foot wear, high body mass index (BMI), occupation, life style, duration of heel pain and female gender are involved in the etiology and may affect the outcome<sup>[4,8-12]</sup>.

The most commonly described therapies are steroid injections, non-steroidal anti-inflammatory drugs (NSAID), exercises, heel pad, and night splint and in intractable cases surgical procedures.

This study was planned to identify the relation between conservative treatment (steroid injection, exercise, heel pad) and duration of pain in plantar fasciitis.

## PATIENTS AND METHODS

During a 12-month period (from July 2004 to June 2005) 75 patients with heel pain syndrome entered the trial. The majority of patients (n = 43) were recruited from the outpatient clinic of King Hussein Medical Center. An additional 32 patients were recruited from the Prince Rashed Military Hospital.

Diagnosis was made from patient's history and physical examination. The following demographic characteristics were recorded at base line (age, sex, BMI, duration of heel pain and occupation).

The study was designed as a therapeutic trial (a prospective cohort study). Patients with foot deformity and pregnancy were excluded from study. The patients were classified into one of two groups: Group 1- patients with less than eight weeks heel pain duration and Group 2 – patients with more than eight weeks heel pain duration. They were not treated previously with same technique but had received analgesics. All patients received the following at their first visit:

- Silicon heel pad for the affected foot to be used while walking and for six months (the duration of the study).

- Methylprednisolone 20 mg/0.5 ml with one ml lignocaine HCL 20% given in the medial aspect of the heel pad and the needle was directed toward

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**Table 1:** Group wise distribution of patient characteristics and symptoms.

Patient group	Heel pain duration	No. of involved heel	Mean age (years)	Mean pain duration	Mean initial pain score	p-value
I	< 8 weeks	32	46	5 weeks	6.3	< 0.001
II	> 8 weeks	45	50	90weeks	6.2	< 0.001

**Table 2:** Group wise distribution of baseline and follow-up pain scores at one, three and six months.

Patient Group	Heel pain duration	No. of involved heel	baseline	p-value	1 month	p-value	3 month	p-value	6 month	p-value
I	< 8 weeks	32	6.3	< 0.001	3.5	< 0.001	2.5	< 0.001	1.2	< 0.001
II	> 8 weeks	45	6.2	< 0.001	4.6	< 0.001	3.8	< 0.001	2.9	< 0.001

the most painful area.

The patients were instructed:

- To avoid bare-foot walking on hard surfaces.
- Non-weight bearing stretching exercise to plantar fascia.
- Strengthening exercises of the intrinsic muscles of the foot (using towel curls, marbles pickups, and toe taps) maintained for 10 minutes, three times daily, for 12 weeks.

Patients were asked by the doctor to score their pain according to the visual analogue scale (VAS) of heel pain as baseline; also immediate pain after injection was scored.

The patients were followed up for outcome measurements over three clinic visits at one, three and six months by the same doctor. At the end of this trial patients were interviewed and asked if they still complained of pain or were cured by the trial treatment. Statistical analysis was done using the SPSS program. Student's t-test was used to compare the results between two groups of study.

## RESULTS

Seventy-five patients were entered into the study; the number of involved heels was 84. Nine out of 75 patients had bilateral symptoms (12%), and the remaining 66 patients had unilateral symptoms. Five patients with seven heels were lost to follow up, so that their outcome measurements were unknown to us. Seventy patients with 77 heel pain continued with their follow up. The study subjects were predominantly female (48 patients, 69%). The patient's age ranged between 36-60 years while the mean age was 48 years. Group 1 had 32 patients with mean heel pain duration of five weeks (range 3-8 weeks) while Group 2 had 45 patients with mean heel pain duration of 90 weeks (range 10-208 weeks). The base line pain scores for Group 1 and 2 were 6.3 and 6.2 respectively. The mean baseline pain score and mean pain score at one, three and six months are shown in Table 2.

There was a marked improvement of pain score in both groups at one month interval; it was more obvious in the first group (3.5) than in the second

group (4.6).

While interviewing the patient during the clinical visit at three and six months, there was a significant improvement in pain score in the first group (2.5, 1.2 respectively) and minimal improvement in the second group ( 3.8, 2.9 respectively).

No relationship was found between (BMI) and pain reduction at one month interval ( $p = 0.3$ ). There was no correlation between patient's age and pain score ( $p = 0.3$ ). No heel infection or plantar fascia rupture were reported among our study. There was no correlation between patient's occupation and pain score ( $p = 0.3$ ).

## DISCUSSION

Conservative treatment of plantar fasciitis is successful when treatment is started within six weeks after the onset of symptoms<sup>[13]</sup>. The earlier the patient present, the more likely that conservative measure will help. This can prevent long standing heel pain and complications which lead to degenerative changes of proximal plantar fascia.

Intrinsic muscles exercises have been advocated. Stretching and strengthening program plays an important role in conservative treatment. It can correct functional risk factor such as: tightness of gastrosoleus complex, weakness of the intrinsic foot muscles and increasing flexibility of calf muscles<sup>[1,14]</sup>.

Recent evidence suggests that non-weight-bearing stretching exercises to plantar fascia provide improvement in pain and mobility compared to weight bearing achilles tendon stretching exercises. When stretches were combined with the use of heel cup, up to 95% patients improved. Orthosis made of soft materials provide cushioning by reducing the shock on walking by up to 42%. Shoes should have an arch support and cushioned heel<sup>[15-17]</sup>.

Steroid injection can provide short pain relief. An injection is best given from medial rather than the inferior aspect of the heel<sup>[15]</sup>. The analysis did not detect relation ship between pain reduction and patient (age, BMI, occupation) and according

to these findings, patient heel pain does not benefit from weight loss. We find that plantar heel pain predominantly affects adults, often in mid to late life with a female predominance.

The loss to follow up of seven heels (5 patients) at one month was insignificant and did not affect the trial. There was no difference between the two groups of patient at the time of injection and first visit. This explains the short term effect of steroid therapy. There was significant improvement in Group 1 patients at three and six months. The slight improvement in Group 2 is explained by the effect of exercise and the use of heel pad which reduce plantar fascia tension and provide shock absorption.

In conclusion, the present study demonstrates that the early diagnosis and treatment (three arm trial therapy of steroid, heel pad, and exercises) could prevent long standing heel pain in more than 95% of patients.

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## Original Article

## Analysis of Hand Fractures in Kuwait

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## ABSTRACT

**Objectives:** To analyze hand fractures in Kuwait and to detect any findings that characterize our population

**Design:** A retrospective study

**Setting:** Al-Razi Hospital, Kuwait

**Subjects:** All patients with hand fractures seen in the hand unit in 2005 were included in this study.

**Main Outcome Measures:** Incidence of hand fractures, site and location of fracture

**Results:** The annual incidence of hand fractures was 93.5 per 100,000 individuals. The age group 25-34 years had 35.6% of fractures and represented the biggest group in carpal, metacarpal and phalangeal fractures. The male to

female ratio was 5:1 and the right to left hand ratio was 1.2 : 1. Non-Kuwaiti nationals had 61% of fractures and 66.7% out of them sustained their fractures at work. The little finger is the most frequently injured finger and the terminal phalanx is the most frequently injured bone. In children the majority of fractures occur at home and crush injury was the mechanism in 79.9% of children four years old and younger.

**Conclusion:** Our results show that a high percentage of fractures occur in non-Kuwaiti nationals at work and there is a high male to female ratio. This is partly explained by the composition of the population in Kuwait.

KEY WORDS: hand fractures, Kuwaiti nationals, terminal phalanx

## INTRODUCTION

Hand fractures are among the most common fractures of the skeletal system as they represent 17-25% of all fractures<sup>[1-3]</sup> and 18-46% of all hand and wrist injuries<sup>[4-6]</sup>. In Kuwait we have no data on the number of hand fractures or their distribution in the hand and in the population. We, therefore, made this study to shed some light on this subject and to try to identify the groups at risk for these fractures and to compare the findings in our population to those in other countries.

## SUBJECTS AND METHODS

A special register was made to include all patients with hand fractures referred to the hand unit in Al-Razi hospital in Kuwait during the period from first of January to 31<sup>st</sup> of December 2005. All the required information was registered on a one-page form completed by the hand surgeon on the first visit to the clinic. This hand surgery unit is the only hand unit in Kuwait and all patient with hand fractures are referred to us except some who are seen by orthopedic surgeons in general and private hospitals. The information collected included age and sex of the patient, hand dominance, anatomical site of the fracture, location of the fracture occurrence and the nationality of the patient.

## RESULTS

During the study period a total of 2796 patients with hand fractures were seen in our hand unit. This gives an annual incidence of 93.5 per 100,000 as the total population of Kuwait at the end of the year 2005 was 2,991,189. The right hand is injured in 53.3% of cases, the left hand in 46% and both hands are injured in 0.7%, with 98.1% of the patients being right-handed.

The average age for all patients was 28.1 years. The average age for men was 29.2 years and that for women was 22.8 years. The age group distribution of hand fractures is shown in Table 1. Patients in the age group 25-34 years had the largest proportion of hand fractures (35.6%) compared to the other groups. This same group also had the largest proportion of carpal, metacarpal and phalangeal fractures with only multiple fractures more common in the age group 45-54 years.

The gender distribution shows that men get the greatest proportion of hand fractures with 83.4% compared to women with only 16.6%. This gives a male to female ratio of 5:1. This gender distribution is true for all fractures and is especially true for the carpal and metacarpal fractures (Table 2).

The distribution of hand fractures by nationality (Table 3) shows that non-Kuwaiti nationals, who

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**Table 1:** The distribution of hand fractures by age group and anatomical location

Age group in years	Carpal bone fractures (% of total number of carpal fractures)	Metacarpal bone fractures (% of total number of metacarpal fractures)	Phalanges fractures (% of total number of phalangeal fractures)	Multiple fractures (% of total number of multiple fractures)	Total (% of total number of hand fractures)
0-4	0 (0)	15 (2.6)	99 (5.1)	0 (0)	114 (4.1)
5-14	2 (0.8)	76 (13.4)	299 (15.5)	0 (0)	377 (13.5)
15-24	81 (31.6)	144 (25.4)	224 (11.6)	12 (27.3)	461 (16.5)
25-34	117 (45)	199 (35)	670 (34.9)	9 (20.4)	995 (35.6)
35-44	41 (15.8)	91 (16)	386 (20.1)	8 (18.2)	526 (18.8)
45-54	10 (3.8)	21 (3.7)	200 (10.4)	15 (34.1)	246 (8.8)
55-64	9 (3.5)	21 (3.7)	27 (1.4)	0 (0)	57 (2.0)
65 +	0 (0)	1 (0.2)	19 (1.0)	0 (0)	20 (0.7)
Total (% of total number of hand fractures)	260 (9.3)	568 (20.3)	1924 (68.8)	44 (1.6)	2796

**Table 2:** The distribution of hand fractures by gender and anatomical location

Gender	Carpal Fractures (% of total number of carpal fractures)	Metacarpal fractures (% of total number of metacarpal fractures)	Phalangeal fractures (% of total number of phalangeal fractures)	Multiple fractures (% of total number of multiple fractures)	Total
Male	248 (95.4)	513 (90.3)	1535 (79.8)	35 (79.5)	2331
Female	12 (4.6)	55 (9.7)	389 (20.2)	9 (20.5)	465
Total	260	568	1924	44	2796

**Table 3:** The distribution of hand fractures by age group and nationality

Age group (in years)	Kuwaiti nationals (% within same age group)	Non-Kuwaiti nationals	Total
0-4	73 (64)	41 (36)	114
5-14	277 (73.5)	100 (26.5)	377
15-24	304 (66)	157 (34)	461
25-34	206 (20.7)	789 (79.3)	995
35-44	107 (20.4)	419 (79.6)	526
45-54	70 (28.5)	176 (71.5)	246
55-64	29 (51)	28 (49)	57
65 +	20 (100)	0(0)	20
Total	1086 (39)	1710 (61)	2796

**Table 5:** Anatomical location of hand fractures

Bone fractured	Number of patients	Percentage
Scaphoid	204	7.3
Other carpal bones	56	2.0
First metacarpal bone	59	2.1
Second metacarpal bone	77	2.8
Third metacarpal bone	40	1.4
Fourth metacarpal bone	75	2.7
Fifth metacarpal bone	317	11.3
Proximal phalanx	614	22.0
Middle phalanx	336	12.0
Terminal phalanx	974	34.8
Multiple fractures	44	1.6

represent 66% of the total population in Kuwait, are affected 61% of the time. They are the majority in the age groups (25-34) and (35-44) years. The Kuwaiti nationals represent 39% of cases and are the majority in the other age groups. The distribution of fractures by location of occurrence (Table 4) shows that 43% of patients sustain their fractures at work and 32.9% at home. Kuwaiti nationals sustain their fractures at home in 51.7% of the time and at work in 5.6% of the time. In contrast, non-kuwaiti nationals sustain their fractures at work in 66.7% of the time and at home in 21.1% of the cases.

The distribution of fractures by anatomical location in the hand (Table 5 and 6) shows that the little finger is the most frequently injured finger in the hand with 27.3% and the terminal phalanx to be the most frequently injured bone with 34.8%. Among the metacarpal bones the fifth metacarpal

bone is most affected (55.8%) and among carpal bones the scaphoid bone is most affected (78.5%). The mechanisms of injury are shown in Table 7.

In children 14 years and younger (Table 8 and 9) the little finger is most frequently injured (36.5%) and the proximal phalanx is the most frequently injured bone (36.9%) with the terminal phalanx second (34.0%). Carpal bone fractures are rare representing only 0.4% of cases. In children 65.1% of their hand fractures occur at home with 13.8% at sport and recreation and 5% occur at school. Girls predominate in four years old children and younger (62.3% girls, 37.7% boys) while boys predominate in older age group (66.5% boys, 34.5% girls). Crush injury is the mechanism in 79.9% of cases in children four years old and younger with a home door causing the injury in 43.9% of cases.

**Table 4:** The distribution of hand fractures by nationality and location of fracture occurrence

Nationality	Location of fracture occurrence					Total
	Home	Work	Sport & Recreation	School	Others	
Kuwaiti (%)	560 (51.7)	61 (5.6)	345 (31.7)	25 (2.3)	95 (8.7)	1086 (100)
Non-Kuwaiti (%)	361 (21.1)	1140 (66.7)	140 (8.2)	18 (1.1)	51 (2.9)	1710 (100)
Total	921	1201	485	43	146	2796

**Table 6:** Location of fractures in the hand

Site of fracture	Number of patients	Percentage
Carpal bone	260	9.3
Thumb	366	13.1
Index finger	358	12.8
Middle finger	421	15.1
Ring finger	453	16.2
Little finger	764	27.3
Multiple fingers	174	6.2

**Table 8:** Distribution of hand fractures in fingers in children (< 14 years)

Finger injured	Number of patients	Percentage
Thumb	120	24.6
Index	54	11.0
Middle	68	13.9
Ring	68	13.9
Little	179	36.6

## DISCUSSION

The composition of the population in Kuwait has some characteristics which are reflected in some of our results. One of these characteristics is that the majority of the manual work power in Kuwait is provided by non-Kuwaiti nationals and they represent two thirds of the general population. They represent 61% of cases with hand fractures and 66.7% of these injuries occur at work with only 21.1% occurring at home and 4.1% occur at sports and recreation. In Kuwaiti nationals, on the other hand, only 5.6% of injuries occur at work with the majority of the fractures occurring at home and during sports and recreation. In some previous reports the rate of work accidents was 9-20% [2,7,8]. The anatomical distribution of hand fractures is also affected by the nature of the man-power in Kuwait. Phalangeal fractures are 68.8% of all fractures which is higher than the 46% reported by Hove[1] and the 59% reported by Van Onsellen[3]. Terminal phalangeal fractures represent 34.8% of all fractures and 59.8% of these occur at work. This is probably a reflection of lack of proper training and lack of proper safety measures in the work place. The carpal bone fractures represent 9.3% of hand fractures similar to previous studies[1,3]. The scaphoid fractures are 78.5% of carpal fractures, which is within the wide range of 51-87% reported in previous studies[1,9,10].

**Table 7:** The distribution of hand fractures by mechanism of injury

Mechanism of injury	Number of patients	Percentage
Fall	1101	39.4
Machinery / Crush	1198	42.8
Quarrel	301	10.8
Car accident	74	2.6
Injury by car/home door	122	4.4

**Table 9:** Distribution of hand fractures by anatomical location in children (< 14 years)

Bone Fractured	Number of patients	Percentage
Scaphoid bone	2	0.4
First metacarpal	10	2
Second metacarpal	24	4.9
Third metacarpal	18	3.7
Fourth metacarpal	8	1.6
Fifth metacarpal	31	6.3
Proximal phalanx	181	36.9
Middle phalanx	50	10.2
	167	34

The distribution of hand fractures by age groups shows that 70.9% of cases are in the age group 15-44 years which is similar to the results of Packer and Shaheen[2] (70% of their cases in the age group 10-40 years) and Van Onsellen[3] (67% of their cases in the age group 10-39 years). The male to female ratio of 5:1 is high compared to other studies which report a range of 1.8 : 1 to 3.7 : 1 [2,3,7,11,12]. This also partly reflects the great number of fractures that occur at work and in sports and recreational activity and this is dominated by men in our society. The right to left hand ratio is similar to that reported by Van Onsellen of 1:1[3] but different from that reported by Packer and Shaheen of 2:1[2].

When we consider children in the age group 0-14 years we find our results for the most frequently injured finger and most frequently injured bone to be similar to other reports[13,14] but at much lower rates. In the Vadivelu *et al* [14] study the little finger was injured in 52% of cases and phalangeal fractures represented 59.5% of the hand fractures. The crush injury is the most common mechanism in young children similar to previous reports and the same is true for the gender distribution. The reversal in the sex incidence of these injuries above the age of four years is not something peculiar to Kuwait. In the

Rajesh *et al* study<sup>[13]</sup> girls predominate in children four years old and younger with 66%, whereas boys predominate in older children with 68%. In the Vadivelu *et al* study<sup>[14]</sup> a similar pattern was noted. They explained this as a result of the cultural changes with girls becoming more involved in sports at younger age, while older boys are more involved in contact sports. Another explanation could be that young girls are presumed, falsely, to be less active and are given more freedom to play unwatched and therefore are more liable to get injured.

The annual incidence of hand fractures calculated in our study of 93.5 per 100,000 individuals is to be taken with caution because although we receive the great majority of hand fractures in Kuwait some patients are seen in other hospitals and not referred to us. We could not find any clear report of the incidence of hand fractures in the literature but they are rather reported as part of the incidence of hand injuries. This incidence has a wide range of 147/100,000 to 705/100,000<sup>[5,6]</sup>.

## CONCLUSION

The distribution of hand fractures in Kuwait is different from that in other countries in some aspects. These include the high percentage of fractures at work, the high percentage of terminal phalanx fractures and the high male to female ratio. This is in part a reflection of the composition of the population in Kuwait.

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## Preliminary Report

# Laparoscopic Inguinal Hernia Repair Using the TEP Technique: A Preliminary Report

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### ABSTRACT

**Objectives:** To study laparoscopic hernia repair as a method of treatment for bilateral and recurrent inguinal hernias using the Totally Extra Peritoneal (TEP) technique

**Design:** Retrospective study

**Setting:** Mubarak Al-Kabeer Hospital, Jabriya, Kuwait

**Subjects:** The first 24 patients between the period April 2003 and April 2006.

**Intervention:** Laparoscopic hernia repair using the TEP technique

**Main Outcome Measure:** Indications for operation, operative time, hospital stay, and postoperative outcome

**Results:** The mean age of our patients was 47 years

(33 to 69 years). Six were recurrent hernias, 16 were bilateral hernias, and two patients had recurrent bilateral hernias. The postoperative hospital stay was one day in the majority of patients ( $n = 20$ , 83.3%), three patients stayed for two days and only one patient stayed for three days. Two patients had some testicular pain, one patient developed urine retention, and one patient developed cord seroma. Seventeen patients (70.8%) required a single dose of analgesia postoperatively.

**Conclusion:** TEP laparoscopic technique for recurrent and bilateral hernias is safe, with a short hospital stay and minimal complications.

KEY WORDS: laparoscopic repair, recurrent inguinal hernia, TEP

### INTRODUCTION

Laparoscopic minimally invasive procedures are gaining popularity. This includes laparoscopic hernia repair, which is now less controversial and more readily acceptable. Numerous technical modifications were described in an attempt to identify the best procedure<sup>[1]</sup>.

Over the past fifteen years, laparoscopic herniorrhaphy became an acceptable procedure. However, it was reported that young patients in whom it is advantageous to avoid a mesh should not undergo this procedure<sup>[2]</sup>. Many studies showed the superiority of laparoscopic hernia repair over open tension-free repair, as described by Gilbert and Lichtenstein, regarding the postoperative pain, early return to work, hematoma formation, and nerve injury. However, it is more expensive and more difficult to learn<sup>[3,4]</sup>.

Two major techniques are used for laparoscopic hernia repair: the transabdominal preperitoneal (TAPP) and the totally extraperitoneal (TEP). For unilateral hernias, the base-case analysis and most of the sensitivity analysis suggested that open-

flat-mesh is the least costly option but provides less quality adjusted life-years (QALYs) than TEP or TAPP<sup>[5]</sup>. For the management of symptomatic bilateral hernias, laparoscopic repair would be more cost-effective with less operative time and shorter hospital stay compared to open mesh repair. However, TEP repair is considered more cost-effective but more technically demanding<sup>[6]</sup>. This is a retrospective review of the TEP technique in the first 24 patients in our unit.

### PATIENTS AND METHODS

This retrospective study includes the first 24 male patients who underwent inguinal hernia repair laparoscopically using the TEP technique between April 2003 and April 2006. A written informed consent was obtained from the patients. All patients underwent the procedure under general anesthesia in the supine position. They received one dose of a third generation cephalosporin antibiotic as prophylaxis. A urinary catheter was inserted in all patients after induction of anaesthesia and was removed at the end of the procedure.

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Three trocars were inserted in the midline. First, an incision was made below the umbilicus through which the posterior rectus sheath space was reached by blunt finger dissection. The camera was introduced and CO<sub>2</sub> insufflation started. The second trocar was introduced under vision through a lower midline incision. Dissection of fibrinous tissue in the preperitoneal space was done and the parietal peritoneum was pushed as cephalad as possible to allow the mesh to lie unfolded in place. The third trocar was inserted through a suprapubic incision.

The inguinal floor was dissected and the anatomic landmarks were recognized. The mesh was introduced and anchored with five staples over the Cooper's ligament and transversalis fascia above the iliopubic tract. Caution was taken not to open the hernial sac or the parietal peritoneum as much as possible. Whenever such an incident happened, the tear was sutured or clipped.

At the end of the procedure, the CO<sub>2</sub> was released while pulling the trocars out. The anterior rectus sheath at the level of the umbilical port was closed. All wounds were closed with intradermal absorbable sutures.

All patients were encouraged to return to their normal activities as soon as their physical condition enabled them to do so.

## RESULTS

The age ranged between 33 and 69 years with a mean age of 47 years. Six patients (25%) were operated for recurrent inguinal hernia, three on the right and three on the left. Sixteen patients (66.7%) had bilateral inguinal hernia. The remaining two patients (8.3%) had combined pathology of recurrent bilateral inguinal hernia. All patients were followed up in the surgical outpatient by the surgical team at two weeks, six weeks, six months, and one year.

The operative time ranged between 40 to 75 minutes, with a mean time of 57.5 minutes. The hospital-stay period ranged from one to two days: 20 patients (83.3%) were discharged on the first postoperative day, three patients (12.5%) on the second postoperative day, and only one patient (4.2%) was discharged on the third day. None of the patients required postoperative sedation. Only 17 patients were given a single dose of indomethacin suppository during recovery.

Complications were minor (Table 1). All patients recovered spontaneously, except the seroma patient, who needed incision and drainage under local anesthesia. No recurrence of hernia was noted at one-year follow-up.

In our view, all patients were fit to return to work at about three days after discharge from the hospital. However, all patients took advantage of the 2-week sick leave allowed by the ministry of health regulations.

**Table 1:** Laparoscopic TEP complications

Complication	n	Percentage
Urine retention	1	4.2
Testicular pain	2	8.4
Cord seroma	1	4.2

TEP: Totally extra peritoneal

## DISCUSSION

Laparoscopic inguinal hernia repair has raised a tremendous amount of controversy since it was introduced. Those who support the procedure argue about the less postoperative pain, early return to work, and better cosmetic results. However, the opponents argue about the higher incidence of complications, recurrence and higher cost compared to open repair. Furthermore, the long term results are unknown<sup>[7]</sup>.

For primary hernias, multi-centric randomized trials revealed no superiority of laparoscopic over open tension-free mesh repair. The recurrence rate was greater than 10% in laparoscopic repair whereas it was less than 5% in open repair. Moreover, the five year recurrence rate after Shouldice repair (6.6%) showed no difference from that of laparoscopic repair (6.7%)<sup>[8,9]</sup>. The open repair of the recurrent hernia is a daunting task because of the already weakened tissues and obscured and distorted anatomy. The failure rate of these repairs using an open anterior approach may reach as high as 36%. Because of such a high failure rate, a number of investigators have focused on repairing these difficult recurrent hernias laparoscopically<sup>[10]</sup>.

The incidents of serious intraoperative complications such as visceral (especially bladder) and vascular injury were found to be more common with less experienced surgeons and with groups who follow the TAPP technique<sup>[11,12]</sup>. Many studies showed less rates of recurrence and overall intra and postoperative complications with the TEP compared to the TAPP techniques. However, TEP has a steep learning curve and is technically more challenging<sup>[13,14]</sup>. The postoperative complications included pain, trocar site hernia, small bowel obstruction and hydrocele. Ninety percent of these complications were in the first 50 cases during the learning period. Previous studies demonstrated that the incidence of significant complications of laparoscopic hernioplasty could be substantially reduced with time and more experience to less than 1%<sup>[15]</sup>.

We adopted the TEP technique as the procedure of choice for both bilateral and recurrent hernias. To overcome the technical difficulties with junior surgeons, the operations were performed by dedicated senior surgeons in our team who have a wide experience in laparoscopic surgery. The results showed that patients did not require any narcotic

sedative. Only a single dose of analgesics was used for 17 cases. There was also faster recovery as noted by discharge from the hospital after one to two days in most cases.

Technically, TEP approach allowed better anatomical orientation of the nerves, the inferior epigastric artery, the pubic tubercle and the internal ring. The mesh was placed from inside the abdominal wall with no tension. Some unsuspected hernias could be discovered intraoperatively and were treated. The TEP also provided a good space to apply meshes of different sizes, up to 15 x 15 cm in some cases. Finally, it treated the hernia at its origin rather than at the site of its presentation.

Recurrence in the literature is always related to less experience and early cases<sup>116,171</sup>. We did not see any recurrence in this study at one-year follow-up. We need to continue for another four years to give the recurrence rate at five years. The complications were minimal. Except for the cord seroma, all resolved spontaneously.

## CONCLUSION

This study showed that the TEP approach for recurrent and bilateral hernia is associated with a low complication rate, and less hospital stay. Our practice is in accordance with the recommendations of National Institute of Clinical Excellence (NICE) which states that open-mesh repair should be the procedure of choice for primary inguinal hernia and that laparoscopic approach should be limited to bilateral or recurrent hernias. Laparoscopic repair may not be a procedure for average general surgeons unless committed to mastering technical expertise<sup>118</sup>.

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## Case Report

# Bloodstream Infection due to *Bacillus Cereus* in a Preterm Neonate Associated with Necrotizing Enterocolitis: A Case Report

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## ABSTRACT

A case of nosocomial bloodstream infection caused by *Bacillus cereus* (*B.cereus*) in a 33-day old preterm neonate in a teaching hospital in Kuwait who developed necrotizing

enterocolitis (NEC) is described. The possible role of *B. cereus* in NEC is discussed.

KEY WORDS: *Bacillus cereus*, bloodstream infection, necrotizing enterocolitis

## INTRODUCTION

*Bacillus cereus* is an emerging pathogen that causes invasive disease in immunocompromised hosts<sup>[1]</sup>. It is a motile, aerobic or facultative anaerobic, spore-forming, gram-positive or gram-variable bacterium of the family *Bacillaceae* that is found worldwide in dust, air, and water. As a human pathogen, the organism is perhaps best known for its role as a mediator of self-limited foodborne illness<sup>[2]</sup>. Although considered a ubiquitous bacterium, the incidence of neonatal infections is very low with only a few cases of *B. cereus* infections in neonates reported in the literature<sup>[3]</sup>. Incidents of nosocomial bloodstream infection in neonates that are caused by this organism have been published mostly as case reports. Some of these reports documented the primary source or the reservoir for infection while others did not<sup>[4]</sup>. To the best of our knowledge, this is the first case encountered of bloodstream infection due to *B. cereus* in a preterm neonate in Kuwait.

## CASE REPORT

The patient was a 28-week preterm female neonate born to a 24-year-old Para 0 + 0 mother who underwent cesarean section. The patient had a birth weight of 840g and an Apgar score of six and eight at one and five minutes respectively. She was ventilated due to respiratory distress and given one dose of exogenous surfactant. She was extubated on day three and placed on Nasal Continuous Positive

Airway Pressure. On day six, she was re-ventilated due to a Patent Ductus Arteriosus (PDA) associated with pulmonary hemorrhage. Umbilical catheters were removed on day 16 and the PDA was ligated on day 17. On day 30, there was a right upper lung lobe collapse on plain radiographs which resolved within three days. Endotracheal secretions showed normal flora.

Breast milk was given on the third hospital day for three days and then resumed on day 15 through day 33 when the patient had repeated vomiting, abdominal distension with discoloration and pneumoperitoneum on plain radiograph (Fig. 1). The WBC count was 14,000, hemoglobin 10.3 g/dl, platelet count 73,000 and C reactive protein was 66 mg/l. Blood cultures were ordered for possible sepsis.

Cultures grew *B. cereus* which was treated with amikacin and cefotaxime. Two pediatric aerobic blood culture bottles were positive for gram positive bacilli 24 hours following incubation using the Bactec System (Becton Dickinson, USA). The isolate showed small beta hemolytic colonies and was a facultative anaerobe, growing well in air at 37 °C. Smears from the culture plates showed gram positive bacilli with infrequent spores which did not swell the bacillary body. The isolate was catalase positive, motile, showed no gas with glucose, non-fermentative with other sugars, and was citrate positive. The isolate showed lecithinase

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Fig. 1: Plain radiograph of the abdomen P-A view showing air under the diaphragm in a preterm neonate with *B. cereus* bloodstream infection who developed necrotizing enterocolitis and jejunal perforation.

positivity on egg-yolk agar and was penicillin resistant but sensitive to clindamycin, gentamycin and vancomycin.

A laparotomy revealed jejunal perforation which was repaired followed by a 17-day course of piperacillin-tazobactam and amikacin. Stool and peritoneal fluid culture after surgery were negative. The patient had zone two stage two retinopathy with no other ocular complications. On day 84, the patient developed *Klebsiella pneumoniae* sepsis and expired the next day. Head ultrasound revealed cystic periventricular leukomalacia.

## DISCUSSION

Due to the widespread distribution of this microorganism, the hospital environment can contain spores of *B. cereus*<sup>[5]</sup>. Drobniowski<sup>[6]</sup> previously reviewed *Bacillus cereus* and related species. He highlighted the role of *B. cereus* as a causative agent of gastrointestinal disease mostly food poisoning and a non-gastrointestinal disease in the form of local infection, ocular infection or systemic disease like bacteremia and septicemia, bacterial endocarditis, central nervous system infection and respiratory infections.

Assessment of the origin of infections may not yield an obvious source. Nonetheless, a few epidemiologic investigations of outbreaks provide some insights on likely vehicles for infections with *B. cereus* in neonatal units. Such vehicles include ventilation equipments<sup>[7]</sup>, IV catheters<sup>[8]</sup>, resuscitation devices, drugs<sup>[9]</sup> or hands of caregivers<sup>[7,9]</sup>. Since our laboratory reported *B. cereus* as the causative agent of bloodstream infection in this preterm neonate, epidemiologic investigation was carried out to identify a potential source of this infection in the NICU. Nonetheless, the source was not identified.

Infection plays an important role in necrotizing enterocolitis (NEC). Frequently NEC is complicated by bacteremia or peritonitis. Putative organisms include *E. coli*, *Klebsiella*, *Salmonella* and *Clostridium spp.* Review of peritoneal cultures from infants undergoing surgery for NEC revealed predominance of *Klebsiella* and *Enterobacter spp.* (63%), *E. coli* (21%), coagulase negative *Staphylococci* (30%), anaerobes (6%) and *candida* isolates (10%)<sup>[10]</sup>. There is one case-report where *B. cereus* was isolated from the peritoneal fluid of a preterm infant who had NEC with perforation<sup>[2]</sup>. It is speculated that the several enterotoxins secreted by the organism may play a role in NEC beside their systemic effects such as septic shock, epidermal necrolysis and alopecia capitis<sup>[11]</sup>. Despite the fact that *B. cereus* bacteremia can be severe with poor prognosis, our patient survived the episode, and stayed alive 52 days thereafter.

## CONCLUSION

Our case report adds new evidence to link *B. cereus* bacteremia to NEC. We speculate that the complications of *B. cereus* bloodstream infection are at least partly related to the effect of *B. cereus*-associated enterotoxins.

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## Case Report

# Spontaneous Pneumothorax in a Patient with Complex Bullous Lung Disease after Blunt Trauma: A Case Report

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### ABSTRACT

The management of spontaneous pneumothorax (SP) in a patient with complex bullous lung disease may be difficult initially. We report a 32-year-old man who presented to the emergency room with head injury after blunt trauma.

The patient had a clinical evidence of SP without chest trauma. He was managed initially with a chest tube but later required surgical intervention to stop the air leak.

KEY WORDS: bullous lung disease, chest tube, pneumothorax

### INTRODUCTION

Spontaneous pneumothorax (SP) can be divided into primary SP resulting from rupture of subpleural blebs, and secondary SP, which is related to the presence of an underlying lung disease (e.g., emphysema and bullous lung disease)<sup>[1]</sup>. The diagnosis and treatment of secondary SP due to bullous lung disease may be difficult initially. The complex appearance of the lungs themselves, partial adherence of the lung to the chest wall, and the clinical presentation may result in an unusual configuration of the pneumothorax or may mask the presentation. Computed tomography (CT scan) is very useful in the diagnosis of bullous lung disease and in the management of complex pneumothorax in such patients<sup>[1,2]</sup>. CT scan will demonstrate the area of pneumothorax, the area of bulla and indicate the best place to insert the chest tube<sup>[2]</sup>.

Numerous therapeutic options are available for the treatment of secondary SP, including chest tube thoracostomy, thoracotomy, and video-assisted thoracoscopic surgery. The indications for surgical treatment include persistent air leak, recurrent SP, and presence of an underlying lung disease<sup>[3]</sup>. We describe a case and the management of a complex secondary SP in a young patient after blunt chest trauma.

### CASE REPORT

A 32-year-old previously healthy Kuwaiti gentleman, smoker, was brought to surgical casualty after a road traffic accident. He suffered

a closed head injury and no other apparent organ injuries. Clinically he had decreased air entry on the right side of the chest and his oxygen saturation was 86%. A chest tube was inserted by open technique for a clinical suspicion of pneumothorax. He was intubated and mechanically ventilated. Subsequently, the lung failed to expand and there was evidence of continuous air leakage. Another chest tube was inserted and connected to low pressure suction (Fig. 1). Urgent CT scan of the chest showed bilateral apical complex bulla and right pneumothorax (Fig. 2). There were no rib fractures and no lung injury. Over the following days, the air leak and right sided pneumothorax persisted and he underwent thoracotomy on day 14 of admission. Multiple bulla on the right side were excised by GIA stapling device (Auto suture Company; United States Surgical Corp, Norwalk, CT). Then, a parietal pleural abrasion by gauze was performed. A 28 F chest tube was inserted and connected to underwater seal suction with a negative pressure of 20 cm H<sub>2</sub>O. Patient was extubated in the operating room and transferred to intensive care unit. The intercostal drain was removed after five days when the underlying lung was fully expanded with no air leakage (Fig. 3).

### DISCUSSION

Primary pneumothorax occurs in young patients with no obvious lung disease while secondary SP occurs when a bulla ruptures in grossly diseased lung and is common in elderly patients. Among

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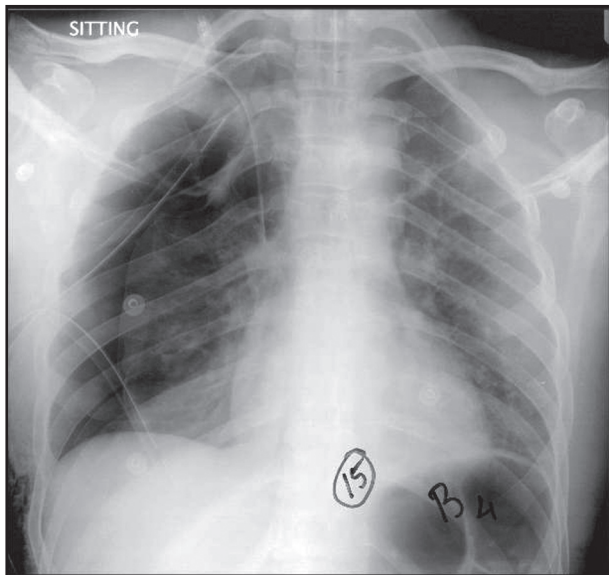


Fig. 1: Postero-anterior chest radiograph showing two chest drains on the right side and pneumothorax

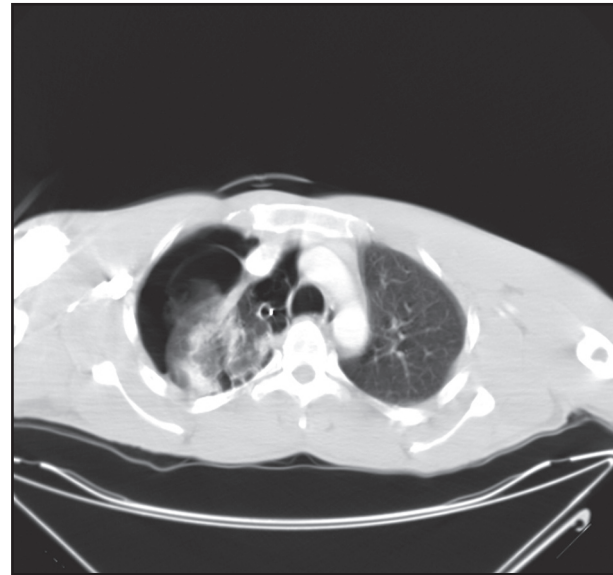


Fig. 2: CT scan of the chest showing pneumothorax on the right side with bulla in the apex of right upper lobe

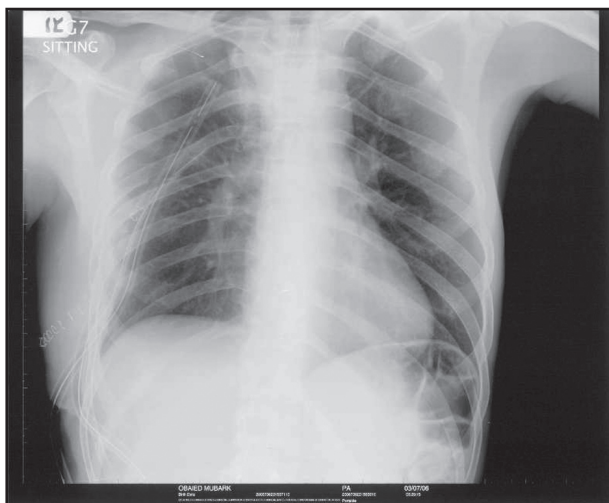


Fig. 3: Postoperative chest radiograph showing one chest drain and fully expanded right lung

the commonest causes of secondary SP are chronic obstructive lung disease (COLD), bullous lung disease and tuberculosis<sup>[1]</sup>. Bullous lung disease is an air-filled space within the lung parenchyma resulting from deterioration of the alveolar tissue. These lesions have a fibrous wall and are trabeculated by the remnants of alveolar septa. They can develop in a lung that is otherwise normal.

We describe a patient with bullous lung disease who had chest trauma and presented with pneumothorax managed initially with chest tube thoracostomy. Further treatment was indicated because of persisting air leak due to presence of a bulla.

Plain chest X-ray is not always reliable in evaluating the extent of pneumothorax and the number and size of the bullae. It might also fail to identify the safe site to insert chest tube. CT scan

can give more information regarding the anatomy and size of the pneumothorax. It can also be useful before surgical intervention<sup>[2]</sup>.

Initial treatment of secondary SP is by inserting a chest tube and if the lung fails to expand, it should be connected to low pressure suction. The American College of Chest Physicians (ACCP) recommended surgical intervention if air leak is persistent for more than 4-7 days in secondary SP<sup>[3]</sup>. Schoenenberger *et al* reported 60% air leak termination rate for chest tube kept for up to 48 hours. Keeping the chest tube for more than two days and up to 10 days did not change this rate. This might suggest a more aggressive approach in treating persistent air leak in secondary SP<sup>[4]</sup>. On the other hand, patients with secondary SP are usually from the older age group and at higher risk from surgery. The ACCP recommended continuing conservative treatment in secondary SP before encouraging the patient to go for surgical intervention. But if the patient is medically fit, surgical intervention might be considered earlier<sup>[3]</sup>.

Persistent air leak is one of the indications for surgical intervention in cases of SP. We believe that the present report is to demonstrate that early surgical intervention is indicated in the management of SP in a group of patients who have complex bullous lung disease. Because of the existence of bullous lung disease and adhesions to the lateral chest wall, CT scan can be done prior to chest tube insertion. This will provide information about the extent of lung disease, the amount of pneumothorax and, the best place for the chest tube insertion.

Tanaka *et al* reviewed 123 episodes of secondary SP and reported 80.5% success rate of non-operative approach while only 19.5% were treated by



thoracotomy. Persistent air leak was the indication for surgical intervention in 62.5% of the patients.

Persistent air leak is commoner in secondary SP compared with the primary SP because of underlying lung disease. Andre's *et al* reported air leak rate of 75% in secondary SP compared with 36% in primary SP<sup>[5]</sup>.

Surgical intervention can be done by open thoracotomy or Video Assisted Thoracic Surgery (VATS). ACCP recommends both methods. Identifying the air leak by thoracoscopy can be difficult because of a smaller field after lung collapse. It can be a cause for persistent air leak postoperatively. Waller *et al* compared the two approaches. For SP the success rate was 97% for thoracotomy and 90% for VATS. All failures were in the secondary SP group. He concluded that VATS was superior to open thoracotomy for primary SP but is less reliable in secondary SP<sup>[6]</sup>.

### CONCLUSION

We advocate the use of CT scan in patients

suspected of pneumothorax in a diseased lung and early surgical intervention in cases of secondary SP.

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## Case Report

# Assessment of Pneumonia Severity

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### ABSTRACT

Pneumonia remains an important cause of hospital admission and carries an appreciative mortality. The diagnosis of pneumonia is based on certain clinical manifestations and chest radiograph. There is considerable variability in rates of hospitalization of patients with

community-acquired pneumonia, in part because of physicians' uncertainty in assessing the severity of illness at presentation. We present a case of pneumonia with certain severity and discuss the methods of assessing severity.

KEY WORDS: community acquired pneumonia, pneumonia, radiograph

### INTRODUCTION

Hospital admission rates for pneumonia vary markedly from one geographic region to the next, suggesting that the criteria used for hospitalization are inconsistent. Physicians often rely on their subjective impressions of a patient's clinical appearance in making the initial decision about the site of care. Physicians tend to overestimate the risk of death in patients with pneumonia and these overestimates are associated with the decision to hospitalize patients at low risk.

Accurate, objective models of prognosis for community-acquired pneumonia (CAP) could help physicians assess patients' risks and improve the decisions about hospitalization. Previous models have been limited by retrospective design, the use of predictor variables about which information is not readily available to physicians when patients present and dependence on complex calculations that are difficult to apply in the clinical setting<sup>[1,2]</sup>. The general applicability of these studies has been limited by the evaluations of performance at single study sites, failure to validate findings in independent patient populations and a nearly exclusive focus on hospitalized patients. Finally, clinical relevance has been compromised by a reliance on mortality as the sole measure of patient outcomes. We will use this case report to discuss how to assess the severity of pneumonia and which patient requires admission to hospital.

### CASE REPORT

A 60-year-old man was admitted to our hospital with three days history of fever, chills and productive cough of yellow sputum. He denied any history of chest pain and gave no history of recent traveling. He was a known case of well-controlled hypertension and diabetes but otherwise healthy.

On physical examination, his heart rate was 120/minute, BP 130/70 mmHg, respiratory rate 28 breath per minute and temperature 38° Celsius. He had no signs of confusion. His chest had right basal crackles. His heart and abdominal examination were normal. His white blood cell count was  $23 \times 10^9/l$ , with a hemoglobin of 120 gram/l and a hematocrit of 38%. His blood urea nitrogen was 14 mg per dl, blood sugar was 200 mg per dl and serum sodium 135 mmol/l. His arterial oxygen tension was 80 mmHg, arterial carbon dioxide tension 40 mmHg and arterial pH was 7.45. Chest X-ray showed right sided air-space disease (Fig. 2). Blood and sputum cultures were negative. He was diagnosed as right lower lobe CAP and was started on cefotaxime and erythromycin intravenously. Two days later, he became afebrile with improvement of his general condition. On the third day oral antibiotics were started and the patient was discharged home after four days of hospitalization on oral clarithromycin. Chest X-ray follow-up after two weeks showed resolution of the pneumonia with no pleural effusion. A chest X-ray two months later revealed complete resolution of the pneumonia.

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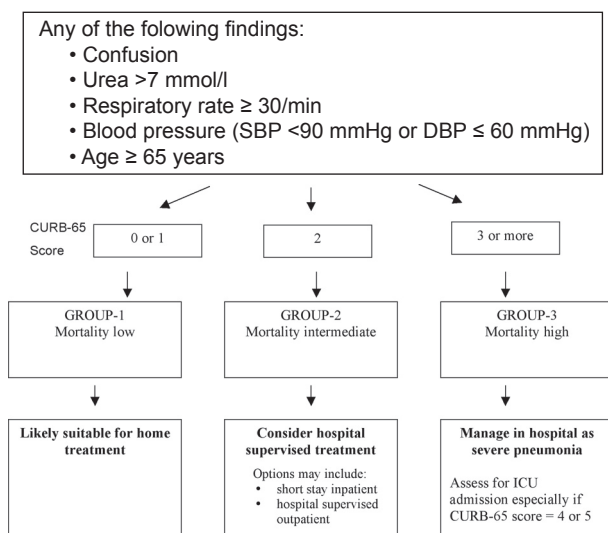


Fig. 1: BTS guidelines for the management of community acquired pneumonia in adults-2004<sup>[6]</sup>

Table 1: Pneumonia severity index for community acquired pneumonia<sup>[3]</sup>

Risk factor	Points
Demographics	
Men	Age (years)
Women	Age (Years) -10
Nursing home resident	+10
Co-morbidities	
Neoplasm	+30
Liver disease	+20
Heart failure	+10
Stroke	+10
Renal failure	+10
Physical examination findings	
Altered mental status	+20
Respiratory rate ≥ 30 breaths per minute	+20
Systolic blood pressure < 90 mmHg	+20
Temperature < 95 °F (35 °C) or ≥ 104 °F (40 °C)	+15
Pulse rate ≥ 125 beats per minute	+10
Laboratory and radiographic findings	
Arterial pH < 7.35	+30
Blood urea nitrogen > 30 mg per dl	+20
Sodium < 130 mmol per l	+20
Glucose ≥ 250 mg per dl	+10
Hematocrit < 30 percent	+10
Partial pressure of arterial oxygen < 60 mmHg	+10
Pleural effusion	+10
Total points	
Risk Class I *	< 51
Risk Class - II*	51 - 70
Risk Class - III*	71 - 90
Risk Class - IV**	91 - 130
Risk Class - V**	> 130

\* Outpatient therapy should be considered for these patients

\*\* Patients should be hospitalized

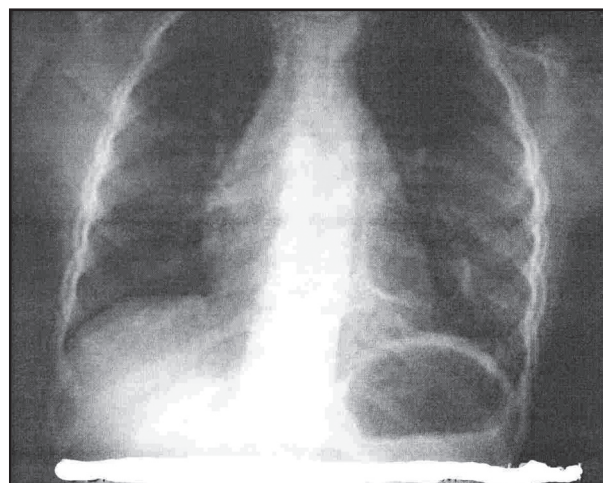


Fig. 2: Right lower lobe pneumonia

DISCUSSION

CAP is often managed outside the hospital, an approach endorsed by evidence-based guidelines from the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA)<sup>[1,2]</sup>. These guidelines however, recommended that physicians make an objective risk assessment using a prospectively validated clinical prediction tool to help guide them when deciding on inpatient or outpatient treatment. The most notable of these tools are the Pneumonia Severity Index (PSI) and several variations of the British Thoracic Society (BTS) rule, such as the CURB-65 (Confusion, Urea nitrogen, Respiratory rate, Blood pressure, 65 years of age and older) score.

The PSI (Table 1) identifies three distinct risk classes (I, II and III) of patients who are at sufficiently low risk for death and other adverse medical outcomes that physicians can consider outpatient treatment or an abbreviated course of inpatient care for them. All patients 50 years of age or less who have none of the coexisting illnesses or physical-examination abnormalities identified (class I) should be candidates for outpatient treatment. Many patients in risk classes II and III are also potential candidate for outpatient treatment. This strategy should apply to the majority of patients assigned to these two risk classes by virtue of age alone or the presence of a single pertinent coexisting illness or abnormal finding on physical examination or laboratory testing. For the remaining patients in classes II and III for whom treatment at home with oral antimicrobial therapy is judged to be unsuitable, there are alternatives to traditional inpatient care. These include parenteral antimicrobial therapy at home or a short stay (< 24 hours) in a hospital observation unit. Previous studies have suggested that one fifth of all patients hospitalized with pneumonia remain in the hospital after becoming

**Table 2:** CURB-65 and CRB-65 severity scores for community acquired pneumonia<sup>[6]</sup>

Clinical factors:	Points	Remarks
Confusion	1	
Blood urea nitrogen > 19 mg per dl	1	
Respiratory rate > 30 breaths per minute	1	
Systolic blood pressure < 90 mmHg or diastolic blood pressure < 60 mmHg	1	
Age ≥ 65 years	1	
Total points:		
CURB-65 score	≤ 1	Low risk, consider home treatment.
“	2	Short inpatient hospitalization or closely supervised outpatient treatment.
“	3-5	Severe pneumonia, hospitalize and consider admitting to intensive care
CRB-65 score	0	Very low risk of death, usually does not require hospitalization
“	1 & 2	Increased risk of death; consider hospitalization
“	3 & 4	High risk of death, urgent hospitalization

medically stable<sup>[3]</sup>. The risk stratification provided by this rule could also help target low-risk patients at the time of admission for whom rapid conversion from intravenous to oral antimicrobial therapy and early discharge might be appropriate<sup>[4]</sup>. Traditional inpatient care for all patients in class IV and V would have reduced the proportion of patients receiving traditional inpatient care by 31 percent and meant a brief observational hospital stay for an additional 19 percent of those who were treated as inpatients. An additional margin of safety could be provided by amending this strategy to include traditional inpatient care for all patients in classes, I, II, and III who have hypoxemia at presentation (*i.e.*, who have an oxygen saturation of less than 90% or a partial pressure of oxygen of less than 60 mmHg while breathing room air). Special attention to oxygen status is consistent with published criteria for hospitalization and with actual clinical practice<sup>[5]</sup>.

The CURB-65 and CRB-65 scores (Table 2, Fig. 1) are easier than the PSI to calculate and interpret at the point of care. CURB-65 includes only five variables (compared with up to 20 in the PSI), and the CRB-65 score provides a four variable substitute for use where blood testing is not immediately available<sup>[6]</sup>.

The authors of the PSI recommend outpatient therapy for patients in PSI risks classes I and II, physician judgment for those in risk class III and hospitalization for those in risks classes IV and V. The IDAS guideline recommends physicians consider home therapy for patient in PSI risk classes I, II and III. The BTS guide line recommends physicians use the CURB-65 or the CRB-65 when deciding

on inpatient or outpatient treatment. The ATS recommends that physicians use validated clinical decision rules such as the PSI or the CURB-65 tool for judgment but does not define a recommended cut off for hospital admission.

BTS guide line recommend the following:

- Patients who have a CRB-65 score of 0 are at low risk of death and do not normally require hospitalization for clinical reasons.
- Patients who have a CRB-65 score of 1 or 2 are at increased risks of death and hospital referral and assessment should be considered, particularly with score 2.
- Patients who have a CRB-65 of 3 or more are at high risk of death and require urgent hospital admission.
- Patient who have a CURB-65 core of 3 or more are at high risk of death and should be managed as having severe pneumonia.
- Patient who have a CURB-65 score of 2 are at increased risk of death. They should be considered for short stay inpatient treatment or hospital supervised outpatient treatment. This decision is a matter of clinical judgment.
- Patient who have a CURB-65 score of 0-1 are at low risk of death. They can be treated as having non-severe pneumonia and may be suitable for home treatment.

Our patient's CURB-65 score was 0 which makes him a very low risk for death, usually does not require hospitalization and can be treated with oral antibiotics. Also, his calculated PSI is less than



51 which is risk class I. This also confirms that our patient was at of low risk for death and the physician could have considered outpatient treatment.

### CONCLUSION

In this case report, we illustrate the usefulness of utilizing easy-to-use and validated prediction rules for assessment of severity of pneumonia and to make decisions about the need for hospitalization. We encourage physicians to use these simple rules, especially the CURB-65 or CRB-65, in the assessment of patients with CAP.

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## Case Report

# A Rare Case of Congenital Anterior Diaphragmatic Hernia

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Kuwait Medical Journal 2008, 40 (2): 150-152

### ABSTRACT

We report a case of a newborn with the rare anterior diaphragmatic hernia with herniation of the liver into the pericardial sac that posed a diagnostic dilemma in our Neonatal Intensive Care Unit (NICU). An

anterior diaphragmatic hernia should be suspected in any newborn with an anterior mediastinal mass or a pericardial effusion. A MRI of the chest helped to confirm the diagnosis. The relevant literature is reviewed.

KEY WORDS: congenital, diaphragmatic, hernia, neonatal

### INTRODUCTION

Congenital diaphragmatic hernia (CDH) occurs approximately once in every 2000 births<sup>[1]</sup>. Posterolateral defects are the most common accounting for 75-80% of hernias<sup>[2]</sup>. Anterior hernia of the foramen of Morgagni is the most uncommon type of CDH accounting for only 1-6% according to previous studies<sup>[3]</sup>. A defect in the central tendon, the rarest of the CDH entities causes the recognizable triad of bilateral pulmonary compression with or without hypoplasia, massive pericardial effusion without cardiac compromise and an intra-pericardial herniation of the liver<sup>[4]</sup>. One such case who delivered in our hospital and posed a diagnostic problem is reported here.

### CASE REPORT

A preterm baby boy was born normally to a 28 year old P O + 3 + 4 + 3 mother at 35 weeks gestation. Antenatal ultrasound examination at 17 and 20 weeks gestation had detected bilateral pleural effusion. Subsequent serial ultrasound examinations at 22, 24, 26 and 28 weeks showed bilateral pleural effusion with pulmonary hypoplasia and there was suspicion of an eventration of the right hemidiaphragm or a central diaphragmatic hernia with liver herniation into the right side of the chest. Intrauterine pleural aspiration was done and 35 ml of fluid was removed which was reported to be serous inflammatory fluid. Amniocentesis confirmed 46XY karyotype. At 33 weeks gestation, pericardial effusion was detected in addition to

the above findings. Parents were counseled about the poor prognosis. A baby boy weighing 2.650 kg was delivered normally at 35 weeks gestation. He required immediate intubation for irregular gasp like respiration. Initial chest X-ray showed bilateral pleural effusion (Fig. 1). As ventilation was difficult, bilateral thoracentesis was done. Fifty milliliter of xanthochromic fluid was removed from the left side and less than 10 ml from the right side. He developed bilateral pneumothoraces which were drained. At 10 hours of age he was shifted to high frequency oscillatory mode of ventilation.

An ultrasound examination of the thorax on day two and nine showed re-accumulation of the pleural fluid on both sides. Computed tomography (CT) scan of the chest on day 8 was reported as loculated air collection in the anterior chest cavity with thin septae compressing the mediastinal structures and both lungs posteriorly and shifting the heart to the left. Echocardiography on day 16 was reported as near systemic pulmonary hypertension, poorly contracting dilated right ventricle and a moderate pericardial effusion. Cardiologist advised conservative management as he was hemodynamically stable. TC 99 lung perfusion scan on day 20 revealed poor uptake in the right lower lobe with poor perfusion and a normal left lung, suggesting a focal pathology in the right lower lobe.

High resolution CT scan of the chest done on day 23 revealed a fluid filled cyst in the anterior mediastinum and bilateral dependant atelectasis

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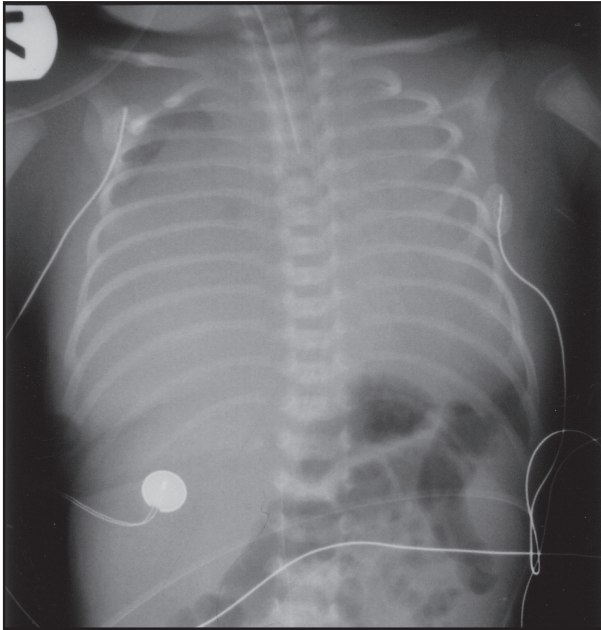


Fig.1: Initial chest X-ray showing bilateral pleural effusion



Fig.2: Postoperative chest X-ray showing the right para-cardiac mass and the bowel loops in the lower mid-thorax

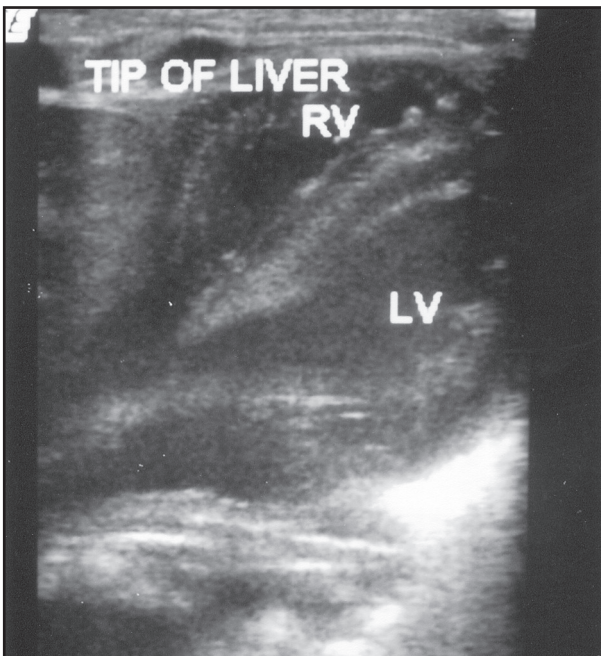


Fig.3: Post operative chest ultrasound showing the liver herniation

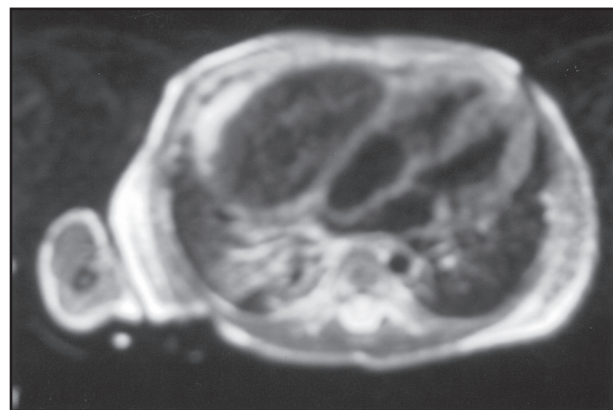


Fig.4: MRI chest showing the liver adjacent to the heart

with pneumonic consolidation of the right lower lobe. Thoracic surgical consultation was sought. An exploratory left thoractomy was done on day 36. At operation a large pericardial effusion was detected. 200 ml of green coloured pericardial fluid was drained. Left hemi-diaphragm and thymus were reported normal. A pericardial window was made. Post-operative chest skiagrams showed clearing of the cardiophrenic angles but a rounded opacity in the right lower zone contiguous with the right cardiac border was more clearly visible (Fig. 2). In some of the post-op CXR films bowel loops could be seen extending up to the lower mid-thorax. He

continued to be ventilator dependant.

A repeat ultrasound examination of the chest on day 45 showed evidence of the liver herniation into the anterior mediastinum through a defect in the anterior diaphragm measuring 4.2 cms (Fig. 3). A MRI chest done on the same day confirmed the liver herniation into the anterior mediastinum (Fig. 4) and he was referred abroad for surgery.

On day 100, a patch repair of the central diaphragmatic hernia and a fundoplication was done. He was successfully extubated and sent back to Kuwait.

## DISCUSSION

The foramen of Morgagni (space of Larrey) extends from the sternum medially to the 8<sup>th</sup> rib laterally and Morgagni hernia occurs because of the failure of complete fusion of the sternal and costal parts of the hemi-diaphragm<sup>[1,5]</sup>. The most



commonly herniated viscera are the liver, spleen and the omentum. Large and small bowels are less commonly seen. Among Morgagni hernias, a particularly rare form is a central defect involving both the diaphragm and the pericardium and in these cases the viscera herniate into the pericardial sac<sup>[1]</sup>. These hernias are believed to represent the developmental failure of the retrosternal position of the septum transversum<sup>[2]</sup>. Presentation may be with respiratory distress and cyanosis soon after birth or with a massive pericardial effusion without cardiac tamponade<sup>[2]</sup>. This suggests the slow formation of the pericardial fluid with compensatory progressive distension of the fetal pericardium. The accumulation of fluid may be due to mechanical irritation of the pericardium<sup>[2]</sup> and a compromised hepatic venous outflow involving the herniated liver (Budd-Chiari like effect)<sup>[4]</sup>.

The postero-anterior and lateral CXR are diagnostic of Morgagni hernia, if the hernial sac contains air filled bowel loops above the diaphragm. This can be confirmed by an upper GI series or a barium enema<sup>[6]</sup>. But, the diagnosis could be difficult if the viscera above the diaphragm are solid with liver or omentum, confusing it with a low anterior mediastinal mass<sup>[6]</sup>. A well defined shadow in the right cardiophrenic angle may be seen on a PA CXR film as was seen in this case after the pericardial fluid was drained. In such cases other diagnostic imaging such as ultrasonography, radionuclide liver / spleen scan, CT or MRI may be needed to confirm the diagnosis<sup>[5,6]</sup>. Liver herniation above the diaphragm can be sonographically distinguished from a pericardial tumor by the appearance of the hepatic vessels coursing into the mass which has the same echogenicity as the liver<sup>[1,7]</sup>.

Echo and CT scan are useful investigations. Continuation of the mass with the liver and the same texture of both shadows help to make the diagnosis of the intra-pericardial herniation of the liver<sup>[8]</sup>.

Though there was suspicion of an anterior diaphragmatic hernia in the earlier antenatal ultrasound examinations, the combination of bilateral pleural effusion and pericardial effusion at the later antenatal ultrasound examinations and the postnatal CXR films made the precise diagnosis of the case difficult. CT scan of the chest done twice and TC 99 ventilation perfusion lung scan did not help in the diagnosis. Once the pericardial fluid was drained at open thoracotomy, the chest X-ray films and ultrasound examination of chest led to the diagnosis of the anterior diaphragmatic hernia which was confirmed by the MRI.

Fetal MRI has been found to be clearly superior to ultrasound in demonstrating the liver herniation into the chest in the antenatal period<sup>[9]</sup>. Emergency

pericardiocentesis and surgery are not always required immediately after birth, even when the condition is suspected by prenatal diagnosis<sup>[10]</sup>.

Morgagni hernias detected in the neonatal period are often associated with congenital anomalies<sup>[11]</sup>. These include congenital heart disease (80%), malrotation (26%), omphalocele (15%) and Down syndrome (14%)<sup>[12]</sup>. This case did not have any other major anomaly.

## CONCLUSION

The possibility of a congenital anterior diaphragmatic hernia with liver herniation should always be considered in the antenatal and post-natal diagnosis of a pericardial effusion or an anterior mediastinal mass. Fetal MRI and post-natal MRI can help in the early diagnosis and optimal management of such cases.

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## Case Report

# Right-sided Pericardio-Diaphragmatic Rupture with Complete Liver and Partial Heart Herniation after Blunt Trauma

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### ABSTRACT

Rupture of the diaphragm and pericardium is an uncommon injury, most frequently caused by high velocity trauma. We present a rare case of right-sided pericardio-diaphragmatic rupture (PDR) with complete

herniation of the liver which prevented the complete herniation of the heart. Diagnostic pitfalls and possible mistakes in the treatment strategy are discussed.

KEY WORDS: cardiac herniation, liver herniation, traumatic diaphragmatic rupture

### INTRODUCTION

Diaphragmatic rupture (DR) occurs in up to 5% of patients sustaining blunt trauma<sup>[1,2]</sup>. Right-sided DR occurs even less frequently (24% of all patients with DR). The herniation of the liver (partial or total) is always present<sup>[3]</sup>. Incidence of the isolated rupture of the pericardium is reported to be 0.08%<sup>[4]</sup>, 25% being on the right side (0.02%)<sup>[4,5]</sup>. We report a case of the right-sided DR with complete herniation of the liver and omentum, accompanied with long right-sided pericardial rupture and intermittent heart herniation.

### CASE HISTORY

A 39-year-old passenger was involved in a road accident. He presented to the local hospital with dyspnea and severe right-sided chest pain. Physical examination revealed a blood pressure (BP) of 80/30 mmHg, variable heart rate of 130-160 beats/min, according to his position, and no evidence of cardiac tamponade. He received intravenous fluids, oxygen and analgesics. Abdominal ultrasound did not reveal free fluid collection. Chest X-ray showed elevation of the right hemi-diaphragm with haziness (Fig. 1). Decision to place a chest tube was made and 800 ml of blood was drained. However the patient's condition worsened, he became hemodynamically unstable, and was transferred to the intensive care unit (ICU). Computed tomography (CT) showed complete herniation of the liver into the right hemi-

thorax (Fig. 2). Soon after, patient became more tachypneic and BP dropped to 60/30 mmHg. His heart rate was very variable – from 120-190 beats/min, depending on patient's position (worsening in the prone and improving in the left decubital position). He required intubation and a decision for emergency right thoracotomy was made.

A posterolateral thoracotomy through the 5<sup>th</sup> intercostal space revealed the whole liver occupying the right hemi-thorax, along with omentum and the chest tube lacerating the liver. After retracting the liver, rupture of the pericardium was seen, extending from superior vena cava to cardiophrenic angle (18 cm long), while the herniating liver was leaning on the heart, preventing it from complete herniation through this defect. Diaphragm was avulsed anteriorly from the chest wall and the rupture extended from anterior to the posterior insertion. Another rupture extended posteriorly from the pulmonary ligament to the costophrenic angle. Herniated liver and omentum were reduced and the diaphragm was reinserted anteriorly to the ribs and sternal periosteum. The tear was repaired using figure-of-eight 0-prolene sutures. The liver laceration was minimal and required only local compression and surgical to control bleeding. Pericardium was closed with 3/0-prolene sutures. The patient had an uneventful postoperative recovery, lung fully expanded and echocardiographic findings were normal.

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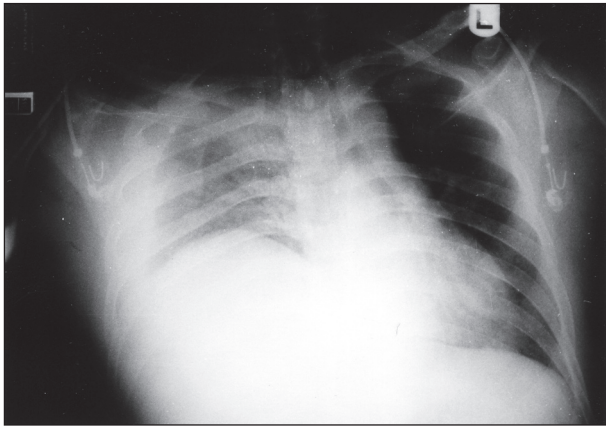


Fig. 1: Chest X-ray showing right hemi-diaphragm elevation with haziness of the right pleural space.

## DISCUSSION

Traumatic diaphragmatic rupture (TDR) occurs rarely – in 0.8-5% of all traffic accident victims and 5% of all trauma patients requiring laparotomy<sup>[3,6,7]</sup>. Involvement of the pericardium is even more rare - 0.2-0.7% of all patients having TDR<sup>[4,8]</sup>. Right sided rupture of the diaphragm, occurs in 25-33% of all patients with this entity, giving a final incidence of 0.05-0.25%<sup>[4,5]</sup>. Isolated rupture of the pericardium (without involvement of any cardiac chamber) is reported to be 0.08%<sup>[4]</sup>, 25% being on the right side (0.02%)<sup>[4,5]</sup>. Only around 70 cases of pericardio-diaphragmatic rupture have been reported so far, 12 lesions of the diaphragm being located on the right side<sup>[9]</sup>, without details about the side of pericardium being involved. Moreover, we believe that this is the first reported case of the total liver herniation along with the partial herniation of the heart.

Associated injuries are present in over 90% of patients, which often dominates the clinical picture, making diagnosis of TDR difficult and of pericardial rupture even more so. Hence, correct diagnosis of pericardio-diaphragmatic injury is missed in up to 66% of multiple injured patients<sup>[3,9]</sup>. Thus, in the absence of other injuries requiring laparotomy and /or thoracotomy, repeat evaluation is necessary to discern injury to the diaphragm or pericardium. Keeping in mind that overall survival after pericardial rupture may be as low as 24%, and for isolated pericardial rupture still only 67%<sup>[4]</sup>, this must be considered a very serious traumatic lesion, that requires prompt diagnosis and immediate treatment. If recognized, treatment is usually simple and effective.

We would like to focus on two details regarding this case. Profound hemodynamical instability of the patient, particularly in the prone position, with immediate rise in the heart rate up to 190 beats / min, and prompt improvement with the patient placed to the left side, should have raised a suspicion that pericardial lesion with the herniation of the heart

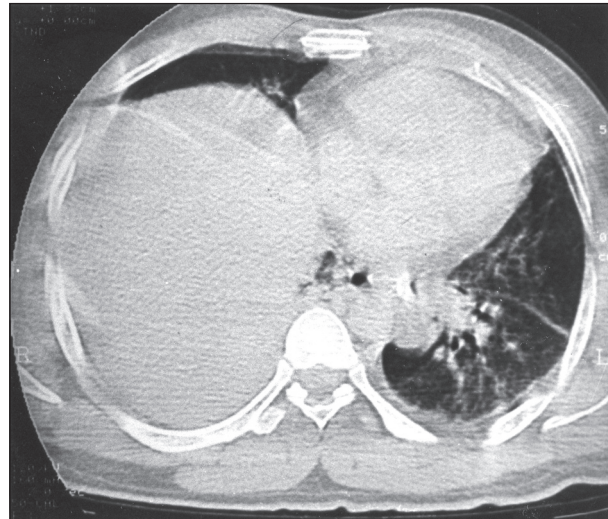


Fig. 2: CT-scan showing complete liver herniation into the right pleural space.

may be present. Secondly, after the placement of the chest tube, the patients' status worsened. Decision to drain the right pleural space was made solely based on the chest X-ray, which proved to be misleading. It has been shown that chest X-ray can be diagnostic or suggestive of diaphragmatic rupture in only 28-70% of cases<sup>[1]</sup>. CT-scan clearly showed the herniation of the whole liver into the right pleural space. This diagnostic method may as well be insufficient, particularly for the right-sided ruptures (correct in only 50% of cases)<sup>[10]</sup>. Without excluding the possibility of organ herniation through the ruptured diaphragm, a chest tube was placed under the wrong assumption that right-sided hemi-diaphragm elevation with haziness is only the collection of blood. Placement of the chest tube, luckily, resulted in only minor liver injury, but could have been fatal otherwise.

## CONCLUSION

We have presented a very rare case of the right-sided pericardio-diaphragmatic rupture, with complete liver herniation and partial herniation of the heart (liver preventing the possibly lethal complete heart herniation). We stress the need for prompt and meticulous diagnosis of this type of lesion, using all available, but most efficient diagnostic tools according to the patients' actual status. Only then, an accurate treatment plan may be devised and favorable outcome expected.

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## Case Report

# Malignant Primary Fibrous Histiocytoma of the Right Ventricle

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Kuwait Medical Journal 2008, 40 (2): 156-158

**ABSTRACT**

We report a rare case of primary cardiac malignant fibrous histiocytoma. A 65-year-old man presented with epigastric tenderness. Echocardiography detected large pericardial effusion and right ventricular mass 5 x 4 cm. Tumor biopsy revealed malignant fibrous histiocytoma.

Thorough investigation did not detect any extra-cardiac primary source or metastasis. Tumor resection was offered to the patient but he refused. Despite refusal the patient was still alive one year after diagnosis.

KEY WORDS: cardiac tumors, fibrous histiocytoma, sarcomas

**INTRODUCTION**

Primary cardiac tumors are rare. Based upon the data of 22 large autopsy series, the frequency of primary cardiac tumors is approximately 0.02%-corresponding to 200 tumors in one million autopsies<sup>[1]</sup>. Majority of the primary tumors of the heart are benign and only about 25% of them are malignant. Of the benign tumors myxoma comprise about 40%<sup>[2]</sup>. The commonest primary malignant cardiac tumors are sarcomas<sup>[3]</sup>. The commonest soft tissue sarcoma in adults is malignant fibrous histiocytoma (MFH)<sup>[4]</sup>.

**CASE REPORT**

A 65-year-old man presented with epigastric tenderness without chest pain, shortness of breath, syncope or presyncope. The patient described weight loss of more than 10 kg in the last few months. His BP on admission was 120/70 and his HR was 100 bpm. JVP was up to the angle of the mandible. There was no lower limb edema. The heart sounds were distant. Chest examination revealed decreased breath sounds at both bases. Abdominal examination showed only mild epigastric tenderness. Electrocardiogram revealed small QRS amplitude and electrical alternans. On chest X-ray, there was enlargement of the cardiac silhouette and small bilateral pleural effusion. Chest and abdominal CT scan detected large pericardial effusion (PE) and bilateral pleural effusions with no abdominal or lung masses. An echocardiography confirmed the large PE. A pericardiocentesis

was done through subxiphoid approach and pericardial biopsy was taken at the same time and a pigtail catheter was left in the pericardial space for about two weeks. The total drainage over that period was about 5600 ml. The pericardial fluid was hemorrhagic. Fluid cultures, Gram stains and AFB were negative. No malignant cells were detected in the fluid. Pericardial biopsy showed chronic inflammatory changes and no sign of malignancy. A repeat echocardiography displayed a large right ventricular mass 5 x 4 cm infiltrating the interventricular septum and extending into the RVOT (Fig. 1). The tumor was cystic in the center. Right ventricular angiography showed filling defect by tumor occupying the inferior and posterior aspect of the right ventricle below the tricuspid valve (Fig. 2). Coronary angiography showed total occlusion of circumflex artery, mild LAD disease. The RCA had 80% proximal stenosis. The right ventricular branch was supplying the tumor and gave it a high vascular network (tumor flush, Fig. 3). A biopsy was taken from the tumor and the result was a malignant fibrous histiocytoma.

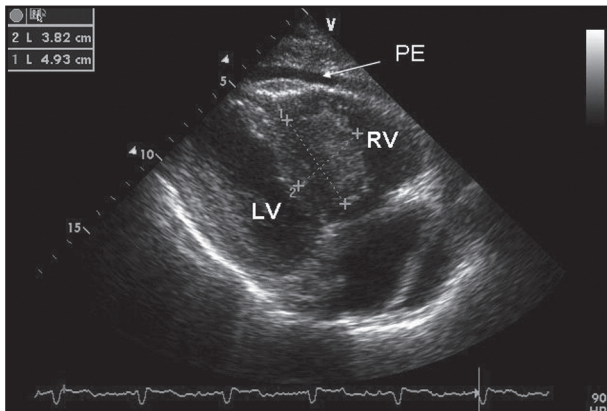
A CT scan done once again to detect any extra cardiac source of the tumor or metastases was negative.

We offered tumor resection with or without chemotherapy but patient refused surgery. Seven months after diagnosis echocardiography was repeated. The tumor was filling the whole right ventricle and extending into the right atrium. It measured 10 x 8 cm in size and the inferior vena

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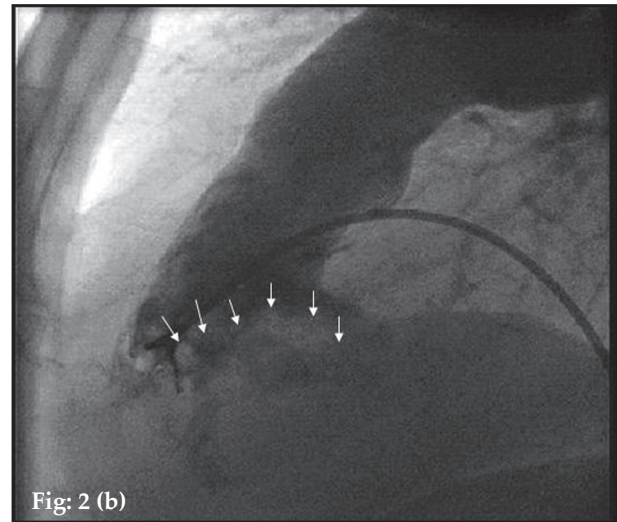
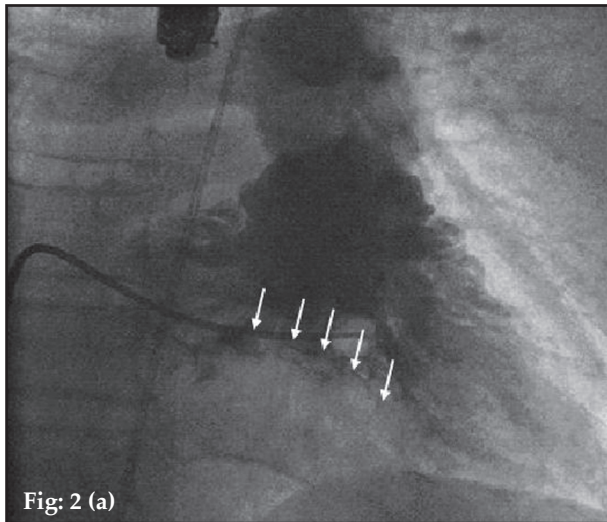


**Fig. 1:** Tumor occupying the right ventricular cavity and measuring 3.8 x 4.9 cm. Also seen is a small pericardial effusion in the anterior pericardial space. PE: pericardial effusion, RV: right ventricle, LV: left ventricle

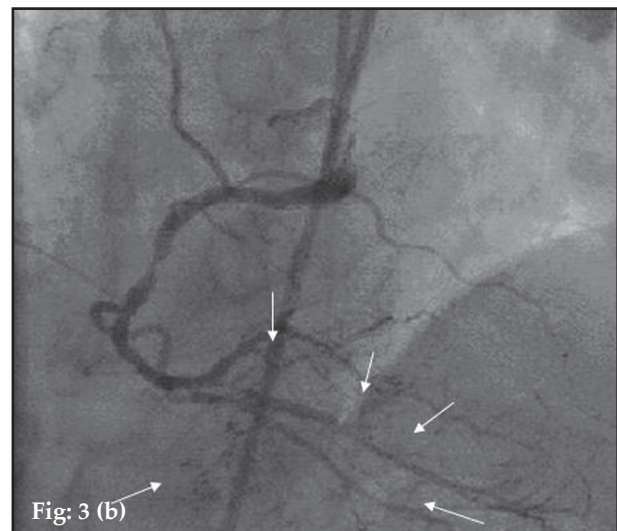
**DISCUSSION**

Primary cardiac tumors are very rare. Their incidence is less than 0.1%<sup>[5]</sup>. More than 75% of them are benign. Metastatic tumors are 20 times more common.

The commonest primary malignancy are sarcomas and the predominant sarcoma is angiosarcoma. MFH is a very rare primary cardiac malignancy. Less than 49 cases are reported in the literature. It was reported first by Shah in 1978<sup>[6]</sup>. Formally they are called pleomorphic rhabdomyosarcomas. Sarcomas in the heart usually involve the right side whereas MFH usually occurs on the left side. Among 47 reported cases 81% were located in the LA<sup>[7]</sup>. Because of this location, the



**Fig. 2:** Right ventricular angiography left lateral projection (a) and RAO projection; (b) The filling defect is seen in both views.



**Fig. 3:** Right coronary angiography LAO projection (a) and LAO cranial view; (b) showing proximal 80% stenosis and vascular network projecting from the RV branch and supplying the tumor.

cava was dilated (28 mm) with minimal respiratory variation. The patient was then lost to follow-up. However, one year after the diagnosis we contacted the patient by phone and found that he was still alive and functional.

symptoms of cardiac MFH are related to pulmonary congestion due to pulmonary vein obstruction, mitral stenosis, mitral regurgitation and right ventricular failure. In our patient the tumor was located in the right ventricle which is an unusual

location for this kind of tumor. It is more common in females and may occur at any age<sup>[7]</sup>.

The disease has very poor prognosis and high recurrence rate. The mean survival is about 12 months<sup>[7]</sup>. Although our patient did not have any kind of treatment for the tumor he survived longer than what was expected. The only proven treatment is tumor resection and it is usually palliative. Chemotherapy or irradiation alone has no proven benefit. It was reported aggressive tumor resection and chemotherapy may offer an extra few months in survival<sup>[8]</sup>.

Although recent malignancy is contraindication for cardiac transplantation<sup>[9]</sup>, this has been reported for cardiac sarcomas<sup>[10,11]</sup>. However, due to limited availability of donor hearts artificial heart transplantation can be an option in selected young healthy patients with no extra cardiac extension.

### CONCLUSION

The diagnostic modality of choice for primary cardiac tumours is echocardiography but CT scan and MRI can be of help in defining the tumor and extent of metastasis. As we put it already, chemotherapy and irradiation alone have no proven benefit and the only proven treatment is tumour resection which is usually palliative.

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## Case Report

# Hereditary Multiple Exostosis Complicated by Popliteal Artery Pseudo-Aneurysm and Common Peroneal Nerve Palsy

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Kuwait Medical Journal 2008, 40 (2): 159-161

## ABSTRACT

We describe a rare case of a twenty-five-year old male patient with a history of hereditary multiple exostoses who presented with a right popliteal fossa swelling and right foot drop following a mild trauma. The swelling proved

to be a popliteal artery pseudo-aneurysm complicating a femoral osteochondroma. The management and surgical treatment are discussed.

KEY WORDS: hereditary multiple exostoses, popliteal artery, pseudo-aneurysm

## INTRODUCTION

Hereditary multiple exostoses is an autosomal dominant skeletal disorder characterized by multiple bony prominences and skeletal deformities. It occurs most commonly around the knee joint, proximal humerus and distal radius. It is the most common skeletal dysplasia, with a frequency of about 1:18,000. It develops in early childhood and becomes obvious with skeletal development<sup>[1]</sup>. Popliteal pseudo-aneurysm is one of the well recognized though uncommon complication of femoral osteochondroma which can occur spontaneously or due to mild trauma but does not necessarily lead to limb ischemia<sup>[2,3]</sup>.

## CASE REPORT

A twenty-five-year old male patient was admitted to our hospital with a large swelling of his right popliteal fossa. The swelling developed after a jerky acute flexion of the right knee joint five weeks ago. The swelling was small and the patient could do his daily activities. However the swelling had increased in size over the last few days and the patient was unable to fully extend his knee and dorsiflex his right ankle. On physical examination there was large, painful deep cystic swelling in the right popliteal fossa with flexion deformity of the knee joint of about 50 degrees (Fig.1). There was also right foot drop but the peripheral pulses were

felt normally. Plain X-ray films showed a giant osteochondroma arising from the posterior aspect of the lower end femur (Fig. 2).

Colored duplex of the popliteal fossa revealed a popliteal artery pseudo-aneurysm arising from the anterior aspect of the artery surrounding a lower femoral giant osteochondroma. CT- angiogram was done which clearly showed the pseudo-aneurysm (Fig.3). 3D-CT showed the rough posterior surface of the osteochondroma (Fig. 4).

Based on history, physical examination, imaging and arteriogram a diagnosis of popliteal artery pseudo-aneurysm was confidently made.

The patient underwent surgery. At operation and after proximal control of the common femoral artery the false aneurysm was excised and the rent in the popliteal artery was repaired directly (Fig. 5, 6). The posterior aspect of the osteochondroma was rough and there was no cartilaginous cap over it. The osteochondroma was excised completely (Fig. 7). We did not explore the common peroneal nerve as we felt that it is a neuropraxia due to compression by the rapidly enlarging pseudo-aneurysm. Postoperative recovery was uneventful and patient was discharged from the hospital after two weeks. During follow-up the patient regained full range of knee movement within four weeks and recovery of the nerve was complete by the sixth month after surgery.

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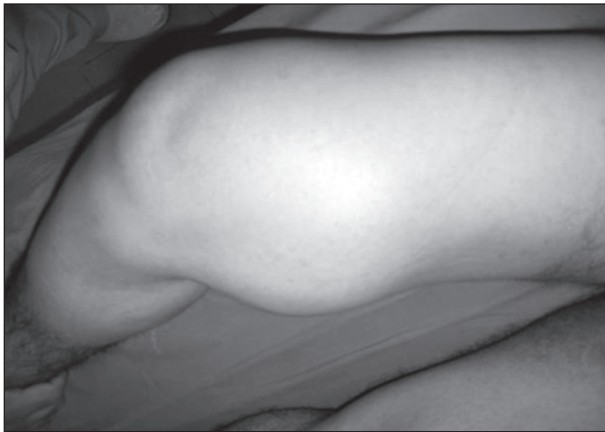


Fig. 1: BTS guidelines for the management of community acquired pneumonia in adults-2004<sup>[6]</sup>

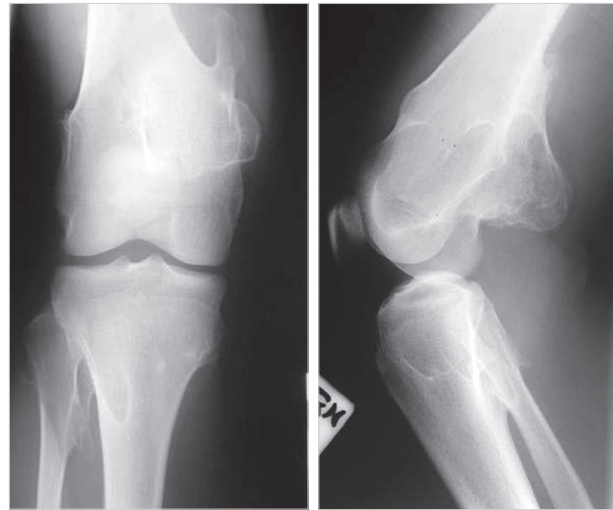


Fig. 2: AP and lateral views showing the osteochondromas in the distal femur



Fig. 3: CT-angiogram showing the pseudoaneurysm pushing the popliteal artery posteriorly

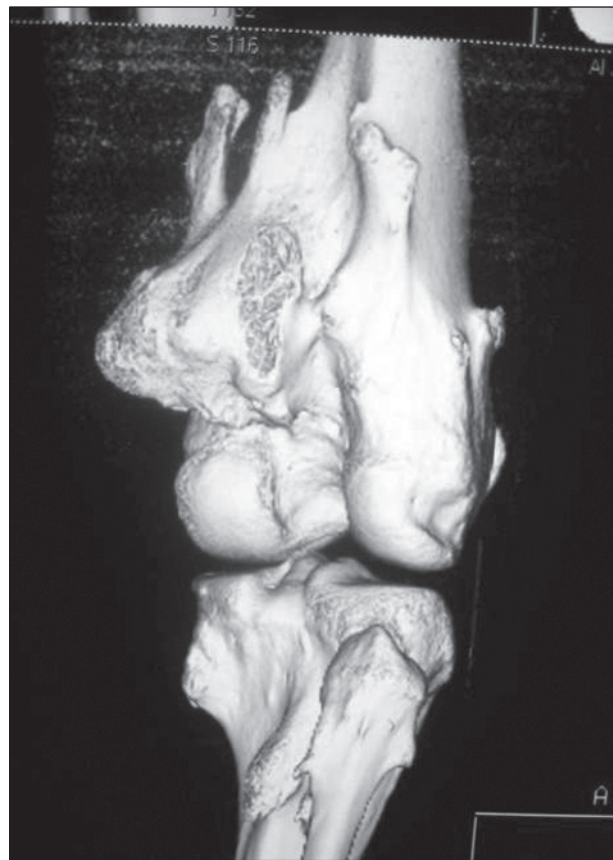


Fig. 4: 3D-CT showing the rough posterior surface of the osteochondroma

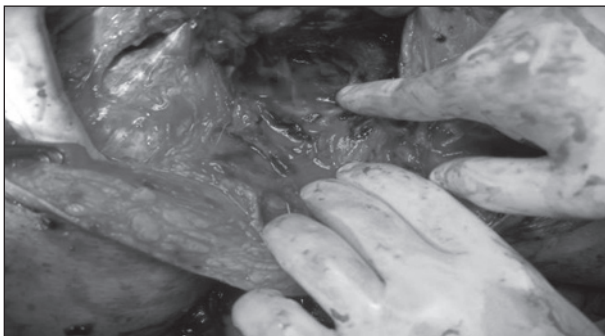


Fig. 5: Intra-operative photograph showing the rent in the artery

**DISCUSSION**

Hereditary multiple exostoses is an autosomal dominant disorder characterized by multiple bony tumors or hamartomas arising near joints. They are cartilage capped and behave in a benign way and are associated with skeletal deformities. Osteochondromas have been reported in all bones but are seen most commonly adjacent to the fastest-growing physes, which are at the distal femur



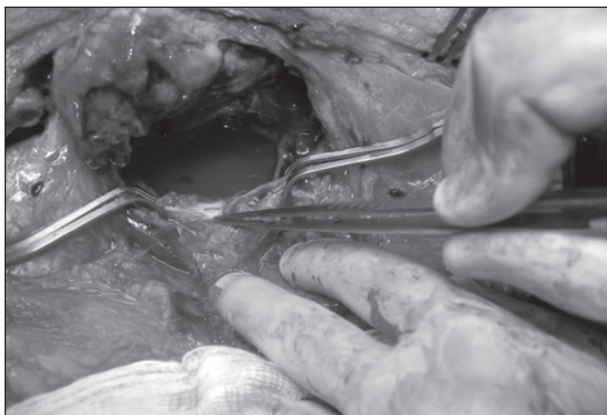


Fig. 6: The blood spurting from the rent in the artery

and proximal tibia. They can lead to mechanical symptoms if the nearby joints, vessels or nerves are involved. Rarely sarcomatous changes can ensue<sup>[1,4]</sup>.

Osteochondromas can lead to a series of complications including fractures through the tumor pedicle, mechanical block of nearby joints, nerve compression and malignant change. Vascular complications are well known but rare and include false aneurysms, arterio-venous fistulae, luminal stenosis and acute ischemia. Venous complications are very rare and include deep venous thrombosis and compression<sup>[5-8]</sup>.

The formation of false aneurysm is due to repeated trauma to the arterial wall by a rough spike of a nearby osteochondroma leading to adventitial tear and the formation of pseudo-aneurysm<sup>[9]</sup>. In our case the posterior aspect of the osteochondroma was found to be rough and there was no cartilagenous cap over it. Thus the vessels were unprotected and became injured by the rough osteochondroma. The common peroneal nerve injury may be due to compression of the nerve by the enlarging tense swelling.

The treatment of popliteal pseudo-aneurysm is exploration of the popliteal fossa and surgical excision of the osteochondroma and the false aneurysm and restoration of the continuity of the artery either by direct repair of the rent in the artery or by-pass surgery. Some authors suggest prophylactic removal of the exostoses, if it lies along the axis of an artery<sup>[5]</sup>.

## CONCLUSION

We believe that preventive intervention must be kept for any suspicion of malignant changes or serious mechanical or vascular compromise. Colored Doppler ultrasound and tridimensional CT may help in proper decision making. If the osteochondroma is in close relation to a major vessel and the surface



Fig. 7: Post operative X-ray, after excision of the osteochondroma

of the osteochondroma facing that vessel is rough as shown by the 3D-CT, it is wise to resect this lesion to avoid serious vascular complications.

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## Selected Abstracts of Articles Published Elsewhere by Authors in Kuwait

Kuwait Medical Journal 2008, 40 (2): 162-167

### Secular Trends in Susceptibility Patterns of Mycobacterium Tuberculosis Isolates in Kuwait, 1996-2005

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*Int J Tuberc Lung Dis.* 2008; 12:319-325

**Objective:** To determine the incidence and trends of drug resistance among all Mycobacterium tuberculosis strains isolated during a 10-year period in Kuwait.

**Design:** Drug susceptibility data for M. tuberculosis isolates recovered from all pulmonary and extra-pulmonary tuberculosis (TB) patients in Kuwait from January 1996 to December 2005 were collected and analysed. Patients were divided into Kuwaiti nationals and expatriates. Prior treatment status was not recorded.

**Results:** From 1996 to 2005, 5399 non-repetitive culture-positive TB cases (56% from pulmonary sites and 44% from extra-pulmonary sites) among 917 (17%) Kuwaiti nationals and 4482 (83%) expatriates were identified throughout Kuwait. Overall resistance rates were as follows: any drug 12.5%, isoniazid (INH) 9.1%; rifampicin (RMP) 1.1%, ethambutol (EMB) 2.0%, streptomycin 4.3% and multidrug resistance (MDR) 0.9%. The resistance rates over the 10-year period remained nearly same. However, significant differences were noted in resistance rates for RMP and MDR among pulmonary vs. extra-pulmonary cases and for any drug, INH and EMB among isolates from Kuwaiti vs. expatriate patients.

**Conclusions:** Moderate and stable single drug resistance (<10%) and low MDR rates (<1%) were found among TB cases in Kuwait. These findings highlight the importance of ongoing control measures to limit the development and spread of drug-resistant M. tuberculosis in Kuwait.

### Psychological Distress and Associated Risk Factors in Bronchial Asthma Patients in Kuwait

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*Indian J Med Sci* 2008; 62:1-7

**Context:** Recent literature shows a high prevalence of psychological distress in bronchial asthma.

**Aim:** To find the extent of psychological distress and associated risk factors in bronchial asthma patients in Kuwait.

**Design:** Case-control study. **Materials and Methods:** In a study at Kuwait's allergy center, 102 patients aged 20-60 years with asthma (67%), asthma with allergic rhinitis (33%) completed a self-

administered questionnaire (WHO-Five Well-being Index). A score below 13 was considered as psychological distress; and 13 and above, as normal. An equal number of controls, matched for age, gender, nationality, were also enrolled.

**Statistical Analysis:** The data were analyzed using SPSS software, and proportions were tested with Chi-square or Fisher's test. Odds ratio (OR) with 95% confidence interval (CI) was calculated to quantify the risk factors. Results: A significantly large proportion (69%) of patients were found to be psychologically distressed, compared to 24% among controls (P).

**Conclusions:** We found a high rate of poor well-being and psychological distress in patients suffering from asthma. Young patients and those with relatively short duration of illness, as well as asthmatic females, are more vulnerable to distress and need further psychological evaluation.

## Spectral Analysis of HIV Seropositivity among Migrant Workers Entering Kuwait

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**BMC Infect Dis 2008; 8:37**

**Background:** There is paucity of published data on human immunodeficiency virus (HIV) seroprevalence among migrant workers entering Middle-East particularly Kuwait. We took advantage of the routine screening of migrants for HIV infection, upon arrival in Kuwait from the areas with high HIV prevalence, to 1) estimate the HIV seroprevalence among migrant workers entering Kuwait and to 2) ascertain if any significant time trend or changes had occurred in HIV seroprevalence among these migrants over the study period.

**Methods:** The monthly aggregates of daily number of migrant workers tested and number of HIV seropositive were used to generate the monthly series of proportions of HIV seropositive (per 100,000) migrants over a period of 120 months from January 1, 1997 to December 31, 2006. We carried out spectral analysis of these time series data on monthly proportions (per 100,000) of HIV seropositive migrants.

**Results:** Overall HIV seroprevalence (per 100,000) among the migrants was 21 (494/2328582) (95% CI: 19 -23), ranging from 11 (95% CI: 8 - 16) in 2003 to 31 (95% CI: 24 -41) in 1998. There was no discernable pattern in the year-specific proportions of HIV seropositive migrants up to 2003; in subsequent years there was a slight but consistent increase in the proportions of HIV seropositive migrants. However, the Mann-Kendall test showed non-significant ( $P = 0.741$ ) trend in de-seasonalized data series of proportions of HIV seropositive migrants. The spectral density had a statistically significant ( $P = 0.03$ ) peak located at a frequency (radians) 2.4, which corresponds to a regular cycle of three-month duration in this study. Auto-correlation function did not show any significant seasonality (correlation coefficient at lag 12 = - 0.025,  $P = 0.575$ ).

**Conclusion:** During the study period, overall a low HIV seroprevalence (0.021%) was recorded. Towards the end of the study, a slight but non-significant upward trend in the proportions of HIV seropositive migrants was recorded. A significant rhythmic cycle of three-month duration was observed in the proportions of HIV seropositive migrants. The underlying factors for a consistent upward trend towards the end of study period and for a significant quarterly cycle in the proportions of HIV seropositive migrants merit further investigations.

## The Importance of Determining the Aggressiveness of Prostate Cancer Using Serum and Tissue Molecular Markers

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**Can J Urol 2008; 15:3967-3974**

Incidental prostate cancer (PCa) has been demonstrated at autopsy in about 80% of men aged 80 years and above and also in 10%-15% of younger men aged 30-50 years in the United States. These data imply a wide variation in aggressiveness of prostate cancer, from indolent tumors to aggressive cancers that kill the patients. The use of prostate specific antigen (PSA) in screening for PCa may detect even indolent disease for which radical prostatectomy may not be necessary. Currently available criteria such as histological grade, PSA level, stage of the disease do not always predict outcome. Furthermore, only about 80% of men with metastatic PCa will respond to first line hormone manipulation and once the patient develops hormone resistant prostate cancer (HRPCa), survival remains poor. Recent genomic and proteomic studies have provided many novel molecular markers that may help to redefine prognostic parameters. This paper is a review of studies using these novel markers in order to determine whether prostate cancer patients with the following characteristics have more aggressive cancer than those without: a) high serum levels of cathepsin B, survivin, Her-2 / neu, IGFBP-2; b) low serum stefin A, IGFBP-3, c) positive immuno-staining of primary tumors for Her-2/neu, survivin and cathepsin B / stefin A ratio > 1 and d) gene expression of AMACR, HER-2/neu, high Bcl-2: Bax ratio and EZH2 in cancer cells. These markers have been chosen for review because they are among the most promising markers emerging currently.

## Geroderma Osteodysplastica/Wrinkly Skin Syndrome: Report of Three Patients and Brief Review of the Literature

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**Pediatr Dermatol 2008; 25:66-71**

Geroderma osteodysplastica and wrinkly skin syndrome are rare autosomal recessive disorders. Due to the many phenotypic similarities in these two conditions, it has been proposed that they represent the same disorder. Both conditions are well delineated in the genetic literature, but despite skin involvement being a striking feature, they are rarely reported in dermatology journals. In this report, we describe three Arab children from two consanguineous families who exhibit overlapping features of geroderma osteodysplastica and wrinkly skin syndrome. All the patients had dysmorphic facial features, wrinkled skin more marked on the hands and feet, hyperextensible joints, intrauterine growth retardation, developmental delay, congenital dislocation of hips, and osteoporosis. Our observations also support the contention that geroderma osteodysplastica and wrinkly skin syndrome have the same clinical spectrum; however, this needs to be confirmed at the molecular level.



## Public Knowledge and Attitudes toward Epilepsy in Kuwait

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**Epilepsia** 2008; 49:564-572

**Purpose:** The study was conducted to determine the familiarity with, knowledge of, misunderstandings, and attitudes toward epilepsy among the Kuwaiti population. **Methods:** A pretested questionnaire was used to collect data from a sample of 784 Kuwaiti individuals, selected from five governorates in Kuwait using a multistage stratified clustered sampling.

**Results:** Seven hundred fifty-five subjects were interviewed, and 97.6% reported their awareness about epilepsy. Of these, 51.8% knew someone who had epilepsy, 56.4% had witnessed an epileptic seizure, 45.9% believed that epilepsy is a hereditary disease, 60.4% reported that "all epileptic fits manifest symptoms of generalized tonic-clonic seizure," 88.3% indicated that putting an object into the patient's mouth to prevent tongue biting during a seizure is appropriate, and 57.1% stated that drug therapy was the only treatment available for epilepsy. Objections to shake hands with, working with, marrying, and employing epileptic patients were reported by 16.0%, 24.8%, 71.6%, and 45.2%, respectively. Childbirth by epileptic women and allowing children to play with an epileptic child were opposed by 56.3% and 27.7%, respectively. A total of 370 (50.2%) agreed that epilepsy is equivalent to psychiatric disorder. **Discussion:** The present findings have demonstrated that epilepsy is a well-known disease in Kuwait, and that negative attitudes toward epilepsy do prevail in Kuwait. The majority of the negative attitudes were significantly associated with the misunderstanding of epilepsy. Continuing effective educational interventions would be needed in order to improve the appropriate understanding of epilepsy, and to ameliorate the social discrimination and misconceptions against epileptic patients.

## Primary Immunodeficiency Disorders in Kuwait: First Report from Kuwait National Primary Immunodeficiency Registry (2004-2006)

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**J Clin Immunol** 2008; 28:186-193

Primary immunodeficiency disorders are heterogeneous group of illnesses that predispose patients to serious complications. Registries for these disorders have provided important epidemiological data and shown both racial and geographical variations. The clinical features of 76 patients with primary immunodeficiency disorders registered in Kuwait National Primary Immunodeficiency Registry from 2004 to 2006 were recorded. Ninety-eight percent of the patients presented in childhood. The prevalence of these disorders in children was 11.98 in 100,000 children with an incidence of 10.06 in 100,000 children. The distribution of these patients according to each primary immunodeficiency category is: combined T and B cell immunodeficiencies (21%), predominantly antibody immunodeficiency (30%), other well defined immunodeficiencies (30%), diseases of immune dysregulation (7%), congenital defects of phagocyte number, function or both (8%), and complement deficiencies (4%). The consanguinity rate within the registered patients was 77%. The patients had a wide range of clinical features affecting different body systems. Primary immunodeficiency disorders are prevalent in Kuwait and have a significant impact into the health system.

## Cytokine Imbalance in Pregnancy Complications and its Modulation

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**Front Biosci 2008; 13:985-994**

The phenomenon of pregnancy can be compromised by a number of complications, such as threatened abortion, recurrent spontaneous miscarriage, preeclampsia, and preterm delivery. Research conducted during the last decade has opened up the possibility that cellular immune effectors may underlie such pregnancy complications. Particularly interesting are the effects of pro-inflammatory and anti-inflammatory cytokines on the conceptus and thus on the success or failure of pregnancy. This review focuses on the association between cytokines and the different complications of pregnancy as well as on the possible pathways of the effector function of cytokines in pregnancy loss. This review also goes on to discuss the redirection of the cytokine profile towards one that is more conducive to pregnancy. Among the most promising agents for the modulation of the Th1/Th2 balance are progestogens such as progesterone and dydrogesterone. Recently published studies lead us to propose that a therapeutic approach worth pursuing would be to assess the individual cytokine profiles of women with pregnancy complications and then to adjust individual therapy using the most effective progestogen.

## Histopathological and Ultrastructural Studies of a Mouse Lung Model of Campylobacter Jejuni Infection

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**J Med Microbiol 2008;57:210-217**

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*Campylobacter jejuni* is a major cause of diarrhoea in humans. However, the pathogenesis of *C. jejuni* diarrhoea is poorly understood due to the lack of a good animal model of infection. Many animals have been tried with limited success, but a mouse lung model of infection has been found to be satisfactory previously; however, the lung pathology of this model has not been studied. For the purpose of characterizing the histopathological and ultrastructural lesions in the lung of the mouse pulmonary model of *C. jejuni* infection, *C. jejuni* strain 81-176 or sterile PBS was intranasally inoculated into BALB/c mice. The infection resulted in a mild illness only, and in an initial predominance of polymorphonuclear cells, followed by the accumulation of macrophages and later the prominence of epithelioid cells. Focal peribronchial pneumonia appeared on day 3, granuloma-like reaction on day 4 and bronchopneumonia on day 5 post-infection. These features developed until day 5 post-infection, but were less consistent afterwards when histopathology was monitored up to 9 days post-infection. Intracellular structures resembling bacteria were observed on days 3 and 5 post-infection, but not on day 7 post-infection. On days 3 and 5 post-infection, degenerative changes were also observed by transmission electron microscopy. The histological changes were not associated with acid-fast bacteria or any fungal elements. The infection was systemic as *C. jejuni* was isolated from blood and all organ homogenates (lung, spleen, liver, and small and large intestines) at 24 h post-infection. Thereafter, the organism was recovered from the intestine only, thus indicating its predilection for this location. This characterization of pathology should contribute to a better understanding of the animal model and pathogenesis of *C. jejuni* infection.

## Patient Demographics and Disease Variables Correlate with Distinct Cytokine Patterns in Mitogen-Stimulated Peripheral Blood Mononuclear Cells from Rheumatoid Arthritis Patients

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**Rheumatol Int. 2008;28:533-539**

There is paucity of literature on the association of peripheral blood cytokine patterns with patient demographics and disease variables in rheumatoid arthritis (RA). We test the hypothesis that there may be differences in peripheral blood levels of inflammatory cytokines in RA subjects according to various disease variables. In this case, we could identify peripheral blood cytokine markers that correlate with different disease variables. Forty-two seropositive RA patients were characterized according to the age at onset, gender, disease duration, severity, activity and ACR functional class. The production levels in mitogen-stimulated PBMCs of five pro-inflammatory cytokines (IFN $\gamma$ , TNF $\alpha$ , TNF $\beta$ , IL-8, IL-18) and three anti-inflammatory cytokines (IL-4, IL-10, IL-13) were evaluated in these patients and in healthy controls. Several new findings emerge: (1) higher levels of IL-4 correlate with female gender, milder disease, non-erosive disease, and earlier age at onset; (2) higher levels of IL-10 correlate with the requirement of  $\leq 2$  DMARDs; (3) higher levels of IL-18 correlate with non-erosive disease and younger age at onset; (4) higher TNF $\beta$  levels correlate with older present age of patients; and (5) higher IL-8 levels correlate with established/late disease. There are several interesting differences in cytokine patterns with respect to age at onset, current age, disease severity, and the number of DMARDs the patients require.

## Forthcoming Conferences and Meetings

Compiled and edited by  
Babichan K Chandy

Kuwait Medical Journal 2008, 40 (2): 168-174

### **Emergency Medicine: An Evidence-Based**

Approach for Improving Outcomes

Jun 01-30, 2008

Sarasota, FL, *United States*

Contact: Eva or Cristina

Tel: 1-866-267-4263 (toll free), 1-941-388-1766; Fax:

1-941-365-7073

E-Mail: mail@ams4cme.com

### **DVD - Dermatology: Recognition and**

Management for Primary Care, Volume III

Jun 01-30, 2008

Sarasota, FL, *United States*

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Tel: 1-866-267-4263 (toll free), 1-941-388-1766; Fax:

1-941-365-7073

E-Mail: mail@ams4cme.com

### **Perinatal Medicine 2008**

Jun 02-04, 2008

Harrogate, England, *United Kingdom*

Contact: Kate Melton

Tel: 02-0-89-798-300 Fax: 02-0-89-796-700

E-Mail: kmelton@hamptonmedical.com

### **4th Annual HIV Up Special Populations, Special**

Needs - **HIV In The Older Adult**

Jun 03, 2008

New York, NY, *United States*

Contact: Eduardo Baez

Tel: 212-746-7187

E-Mail: edb2005@med.cornell.edu

### **Advances in Trauma and Critical Care Surgery**

Jun 04-06, 2008

Minneapolis, MN, *United States*

Contact: University of Minnesota Office of

Continuing Medical Education

Tel: 612-626-7600; Fax: 612-626-7766

E-Mail: cme@umn.edu

### **43<sup>rd</sup> Congress of the Polish Society of**

**Otolaryngologists**

Jun 04-07, 2008

Lodz, *Poland*

Contact: Marcin Durko M.D

Tel: 48-426-785-785; Fax: 48-426-785-785

E-Mail: sekretariat@orl2008.pl

### **Antepartum and Intrapartum Management**

Jun 05-07, 2008

San Francisco, CA, *United States*

Contact: UCSF Office of Continuing Medical

Education, 3333 California Street, Room 450, San

Francisco, CA 9411

Tel: 415-476-4251 / 415-476-5808 Fax: 415-476-0318

/ 415-502-1795

E-Mail: info@ocme.ucsf.edu

### **7<sup>th</sup> Summer Conference on Acute Heart Failure**

Jun 06-08, 2008

Athens, *Greece*

Contact: Estelle Flament

Tel: 32-25-590-355; Fax: 32-25-270-062

E-Mail: congsecre@esicm.org

### **Updates in Clinical UltraSound**

Jun 08-11, 2008

Ravello (SA), Amalfi Coast, *Italy*

Contact: Mrs. Suita Carrano

Tel: 800-0-90-271 / 39-0-89-857-922; Fax: 39-0-89-

858-570

E-Mail: Info@weddingravello.it

### **Egyptian Society of Women's Imaging & Health**

**Care 3<sup>rd</sup> Annual Scientific Meeting**

Jun 08-14, 2008

Cairo, *Egypt*

Contact: Meeting Organiser

Tel: 20-123-938-584

E-Mail: contact@eswih.org

### **The 1<sup>st</sup> International Congress of Infection in**

**Transplantation and Cancer**

Jun 10-12, 2008

Tehran, *Iran*

Contact: Meeting Organiser

Tel: 00-982-122-424-205-10; Fax: 00-982-122-424-206

E-Mail: info@idtmrc.ac.ir

### **Live Symposium of Complex Coronary &**

**Cardiovascular Cases**

Jun 11-14, 2008

New York, NY, *United States*

Contact: CME Office

Tel: 212-731-7950; Fax: 212-731-7930



**26<sup>th</sup> Annual Meeting ESOPRS**

Jun 12-14, 2008

Lucerne, *Switzerland*

Contact: bbs Congress, Bern

Tel: 41-313-318-275; Fax: 41-313-329-879

E-Mail: esoprs.2008@gmail.com

**Food as Medicine**

Jun 12-15, 2008

Baltimore, MD, *United States*

Contact: Klara Royal

Tel: 202-966-7338 ext 241; Fax: 202-966-2589

E-Mail: fam@cmbm.org

**Hong Kong's Shanghai International Liver Congress 2008**

Jun 12-15, 2008

Hong Kong, *China*

Contact: 2008 ILC Secretariat

Tel: 85-228-272-090; Fax: 85-228-272-220

E-Mail: info@cosoman.com

**Heart Failure 2008 Congress**

Jun 14-17, 2008

Milan, *Italy*

Contact: Sabrina Volle

Tel: 33-0-492-947-600; Fax: 33-0-492-947-601

E-Mail: HFsecretariat@escardio.org

**Infectious Disease Update**

Jun 16-27, 2008

Harwich, England, *United Kingdom*

Contact: Eileen Tener

Tel: 813-333-6878

E-Mail: etener@CruisersParadise.com

**CARDIOSTIM - 16<sup>th</sup> world congress in Cardiac Electrophysiology and Cardiac Techniques**

Jun 18-21, 2008

Nice, *France*

Contact: Clarisse Sable

Tel: 33-147-565-084; Fax: 33-147-562-466

E-Mail: cardiostim@reedexpo.fr

**12<sup>th</sup> Annual Conference of Iranian Nuclear Medicine**

Jun 19-21, 2008

Sari, *Iran*

Contact: Meeting Organiser

Tel: 00-981-513-257-230; Fax: 00-981-513-261-244

E-Mail: nm@mazums.ac.ir

**9<sup>th</sup> International Fetal Cardiology Symposium**

Jun 19-21, 2008

Nice, *France*

Contact: Pr GUIRGIS Maurice

Tel: 00-33-665-390-767; Fax: 00-33-146-020-509

E-Mail: guirgis1@hotmail.com

**Glucocorticoids & Mood: Clinical Manifestations, Risk Factors & Molecular Mechanisms**

Jun 20-21, 2008

San Diego, CA, *United States*

Contact: UCSD CME

Tel: 858-534-3940; Fax: 858-822-5908

E-Mail: ocme@ucsd.edu

**2<sup>nd</sup> International Experts' Meeting on Advanced Laparoscopic Surgery**

Jun 20-22, 2008

Athens, *Greece*

Contact: Costopoulou Niki

Tel: 302-106-049-215; Fax: 302-106-049-724

E-Mail: costopoulou.n@congressexcel.gr

**10<sup>th</sup> National Congress on Cardiovascular Update**

Jun 21-25, 2008

Tehran, *Iran*

Contact: Mohammad Hasani M.D.

Tel: 98-21-88-684-430; Fax: 98-21-88-684-430

E-Mail: irsa@email.co

**Update on the Management of Thromboembolic Disorders**

Jun 22-26, 2008

Sacramento, CA, *United States*

Contact: Office of Continuing Medical Education

Tel: 916-734-5390/866-263-4338/866-CME-4EDU

E-Mail: gwenn.welsch@ucdmc.ucdavis.edu

**Current Topics in Noninvasive Cardiovascular Imaging**

Jun 22-27, 2008

San Diego, CA, *United States*

Contact: Mayo Clinic Radiology CME Department

Tel: 1-866-246-1581 or 507-284-3317; Fax: 507-266-3061

E-Mail: scheel.mindy@mayo.edu

**Allergy, Asthma and Immunology Update**

Jun 24-25, 2008

Albany, NY, *United States*

Contact: Albany Medical College's Office of Continuing Medical Education

Tel: 518-262-5828; Fax: 518-262-5679

E-Mail: amccme@mail.amc.edu

**ICI - Imaging in Cardiovascular Interventions**

Jun 25, 2008

Frankfurt am Main Hessen, *Germany*

Contact: Ms Nadine Koebke

Tel: 49-60-789-316-877; Fax: 49-60-789-316-879

E-Mail: nkoebke@convents.biz

4<sup>th</sup> Asian Interventional **Cardiovascular Therapeutics**  
 Jun 25-27, 2008  
 Bangkok, *Thailand*  
 Contact: Mr. Pong  
 Tel: 66-27-180-060-5; Fax: 66-27-180-065  
 E-Mail: thaiheart@thaiheart.org

CSI - 11<sup>th</sup> International Congress **Congenital and Structural Interventions**  
 Jun 26-28, 2008  
 Frankfurt am Main, *Germany*  
 Contact: Ms Nadine Koebke  
 Tel: 49-60-789-316-877; Fax: 49-60-789-316-879  
 E-Mail: nkoebke@convents.biz

ISN Nexus symposium on **Diabetes and the Kidney**  
 Jun 26-29, 2008  
 Dublin, *Ireland*  
 Contact: Michael Podt  
 E-Mail: michael.podt@isn-online.org

**Biosignal 2008**  
 Jun 29 - Jul 01, 2008  
 Brno, *Czech Republic*  
 Contact: Meeting Organiser  
 Tel: 42-0-541-149-558  
 E-Mail: bs2008@feec.vutbr.cz

**Primary Care, Part 1: A Comprehensive Review in Adult Medicine**  
 Jul 01-31, 2008  
 Sarasota, FL, *United States*  
 Contact: Eva or Cristina  
 Tel: 1-866-267-4263 (toll free), 1-941-388-1766; Fax: 1-941-365-7073  
 E-Mail: mail@ams4cme.com

The XII International Congress "**Phytopharm 2008**"  
 Jul 02-04, 2008  
 St. Petersburg, *Russia*  
 Contact: Prof. Valery Makarov  
 Tel: 78-125-452-230; Fax: 78-123-225-605  
 E-Mail: phyto2008@mail.ru

The 1<sup>st</sup> World Congress on Controversies in **Cardiovascular Disease** Diagnosis, Treatment and Interventions (C-Care)  
 Jul 03-06, 2008  
 Berlin, *Germany*  
 Contact: Ms. Ruthi Yahav  
 Tel: 972-3-56-66-166; Fax: 972-3-56-66-177  
 E-Mail: ccare@comtecmed.com

EACR 20 - 20<sup>th</sup> Meeting of the European Society for **Cancer Research**  
 Jul 05-08, 2008  
 Lyon, *France*  
 Contact: Mrs. Davi Kaur  
 Tel: 32-27-750-201; Fax: 32-27-750-200  
 E-Mail: EACR20@feces.be

Seminar on **Legal-Medical Issues**  
 Jul 12-19, 2008  
 Vancouver, BC, *Canada*  
 Contact: Eileen Tener  
 Tel: 813-333-6878  
 E-Mail: etener@CruisersParadise.com

Reconstructive **Vaginal Surgery**  
 Jul 13-14, 2008  
 Vancouver, BC, *Canada*  
 Contact: Christine Morris  
 Tel: 856-427-6200; Fax: 856-427-6202  
 E-Mail: contact@imetcme.com

Techniques & Applications of **Molecular Biology**  
 Jul 14-17, 2008  
 England, *United Kingdom*  
 Contact: Dr Charlotte Moonan  
 Tel: 0-24-76-523-540; Fax: 0-24-76-523-701  
 E-Mail: Charlotte.Moonan@warwick.ac.uk

Seminar on **Legal-Medical Issues**  
 Jul 16-28, 2008  
 Barcelona, *Spain*  
 Contact: Eileen Tener  
 Tel: 813-333-6878  
 E-Mail: etener@CruisersParadise.com

14<sup>th</sup> World Congress on **Heart Disease**, International Academy of Cardiology Annual Scientific Sessions 2008  
 Jul 16-29, 2008  
 Toronto, ON, *Canada*  
 Contact: Meeting Secretariat, 14<sup>th</sup> World Congress on Heart Disease, International Academy of Cardiology, Annual Scientific Sessions 2008, PO Box 17659, Beverly Hills, CA 90209, USA  
 Tel: 1-310-657-8777; Fax: 1-310-659-4781  
 E-Mail: Klimedco@ucla.edu

**Wound Care** SST Specialization, Science, Technology  
 Jul 17-19, 2008  
 Chicago, IL, *United States*  
 Contact: Dennis A. Vitrella  
 Tel: 337-235-6606; Fax: 337-235-7300  
 E-Mail: dennis@woundcaresst.com

**Heart Failure 2008**

Jul 17-20, 2008

Amelia Island, FL, *United States*

Contact: UNC CME Office

Tel: 919-962-2118; Fax: 919-962-1664

E-Mail: Ada\_Southerland@med.unc.edu

**7<sup>th</sup> International Conference on Head and Neck Cancer**

Jul 19-23, 2008

San Francisco, CA, *United States*

Contact: Conference Secretariat: American Head &amp; Neck Society 11300 West Olympic Boulevard, Suite 600, 90064 Los Angeles

Tel: 1-310-437-0559; Fax: 1-310-437-0585

E-Mail: admin@ahns.info

**Medical and Surgical Approaches to GI Disorders**

Jul 21-25, 2008

Kiawah Island, SC, *United States*

Contact: CME Office

Tel: 706-7213967 / 800-221-6437; Fax: 706-721-4642

E-Mail: jstill@mail.mcg.edu

**Seminar on Legal-Medical Issues**

Jul 22-Aug 03, 2008

Southampton, England, *United Kingdom*

Contact: Eileen Tener

Tel: 813-333-6878

E-Mail: etener@CruisersParadise.com

**GCP meeting**

Jul 24-25, 2008

Kiev, *Ukraine*

Contact: Kristina Shevchenko

E-Mail: dr@nbscience.com

**14<sup>th</sup> World Congress on Heart Disease**

International Academy of Cardiology Annual Scientific Sessions 2008

Jul 26-29, 2008

Toronto, ON, *Canada*

Contact: Asher Kimchi, MD

Tel: 1-310-657-8777; Fax: 1-310-659-4781

E-Mail: klimedco@ucla.edu

**Cardiology and Infectious Disease**

Jul 28-Aug 09, 2008

Oslo, *Norway*

Contact: Dr. Martin Gerretsen

Tel: 1-888-647-7327; Fax: 1-888-547-7337

E-Mail: cruises@seacourses.com

**32<sup>nd</sup> Annual Meeting of the Christian****Ophthalmology Society**

Jul 30-Aug 03, 2008

Callaway Gardens, GA, *United States*

Contact: Sterling Cannon, M.D

Tel: 706-478-0764

E-Mail: COScallaway@yahoo.com

**Success with Failure: New Strategies for the Evaluation and Treatment of Congestive Heart Failure**

Aug 03-06, 2008

Whistler, BC, *Canada*

Contact: Mayo School of Continuing Medical Education Office

Tel: 800-462-9633 / 904-953-7114 / 800-323-2688

Fax: 904-953-2954 / 507-284-0532 / 480-301-8323

E-Mail: cme-jax@mayo.edu / cme@mayo.edu

**The XVII International AIDS Conference**

Aug 03-08, 2008

Mexico City, *Mexico*

Contact: General Info

Tel: 41-227-100-800

E-Mail: info@aids2008.org

**Hawaii Anesthesiology Update 2008**

Aug 04-08, 2008

Kohala Coast, HI, *United States*

Contact: Maria Courtney

Tel: 800-328-2308; Fax: 210-641-8329

E-Mail: mariac@dannemiller.com

**XXII International Congress of The****Transplantation Society**

Aug 10-14, 2008

Sydney, NSW, *Australia*

Contact: The Meeting Planners, 91-97 Islington Street, Collingwood, VIC, Australia, 3066

Tel: 61-394-170-888; Fax: 61-394-170-899

E-Mail: tts2008@meetingplanners.com.au

**Echocardiography: The Fundamentals**

Aug 13-15, 2008

Philadelphia, PA, *United States*

Contact: Office of CME · 1020 Locust Street · Suite M5 · Philadelphia, PA 19107-6799

Tel: 1-888-JEFF-CME / 215-955-6992; Fax: 215-923-3212

E-Mail: jchp@jefferson.edu

**12<sup>th</sup> World Congress on Pain**

Aug 17-22, 2008

Glasgow, Scotland, *United Kingdom*

Contact: Elizabeth Twiss

Tel: 206-547-6409; Fax: 206-547-1703

E-Mail: liz@iasp-pain.org

**XXII European Conference on Philosophy of Medicine and Health Care**

Aug 20-23, 2008

Tartu, *Estonia*

Contact: Dr. Bert Gordijn, Secretary of the ESPMH, Dept. of Ethics, Philosophy and History of Medicine 137, Radboud University Nijmegen Med. Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands

E-mail: b.gordijn@efg.umcn.nl

**14<sup>th</sup> International Congress of Immunology**

Aug 22-27, 2010

Kobe, *Japan*

Contact: Prof. Masayuki MIYASAKA

Tel: 81-6-6879-3972; Fax: 81-6-6879-3979

E-Mail: mmiyasak@orgctl.med.osaka-u.ac.jp

**Urology Update for the Non-Urologist**

Aug 22-29, 2008

Seward, AK, *United States*

Contact: Eileen Tener

Tel: 813-333-6878

E-Mail: etener@CruisersParadise.com

**18<sup>th</sup> World Congress on Ultrasound in Obstetrics and Gynecology**

Aug 24-28, 2008

Chicago, IL, *United States*

Contact: Congress Secretariat

Tel: 44-0-2-074-719-955; Fax: 44-0-2-074-719-959

E-Mail: congress@isuog.org

**9<sup>th</sup> International Congress on Reproductive Biomedicine**

Aug 27-29, 2008

Tehran, *Iran*

Contact: Dr. Azadeh Oraei

Tel: 982-122-305-236; Fax: 982-122-310-406

E-Mail: Congress@Royaninstitute.org /

Royancongress@gmail.com

**6<sup>th</sup> International Congress on Autoimmunity**

Sept 03-07, 2008

Porto, *Portugal*

Contact: Jo Jackson

Tel: 41-229-080-488; Fax: 41-227-322-850

E-Mail: autoimmunity@kenes.com

**Intraoperative Echocardiography in the 21<sup>st</sup> Century**

Sep 04-07, 2008

Atlanta, GA, *United States*

Contact: Continuing Medical Education, 1462

Clifton Road, Suite 276 Atlanta, GA 30322

Tel: 1-888-727-5695 / 404-727-5695; Fax: 404-727-5667

E-Mail: cme@emory.edu

**ILCA 2008**

Sep 05-07, 2008

Chicago, IL, *United States*

Contact: Cecilia Waldvogel

Tel: 322-789-2345; Fax: 322-743-1550

E-Mail: info@ilca-online.org

**Organ Imaging Review 2008**

Sep 07-10, 2008

Toronto, ON, *Canada*

Contact: Office of Continuing Education &amp; Professional Development

Tel: 416-978-2719; Fax: 416-946-7028

E-Mail: help-MIM0802@cmeteronto.ca

**STD 7 / Aids 3**

Sep 07-10, 2008

Goiânia, *Brazil*

Contact: Alberto Tiburcio

Tel: 69-32-223-153

E-Mail: josesarahoscar@ibest.com.br

**14<sup>th</sup> World Congress of Psychophysiology**

Sep 08-13, 2008

St.Petersburg, *Russia*

Contact: Dr.Tatiana Denisenko

Tel: 812-335-2055 ext 160; Fax: 812-335-2039

E-Mail: Tatiana.Denisenko@monomax.org

**5<sup>th</sup> International Pediatric Intestinal Failure and Rehabilitation Symposium**

Sep 11-13, 2008

Pittsburgh, PA, *United States*

Contact: Jada Shirriel

Tel: 412-647-8216; Fax: 412-647-8222 / 412-647-1244

E-Mail: shirrielj@upmc.edu

**19<sup>th</sup> Annual Coronary Interventions**

Sep 17-19, 2008

San Diego, CA, *United States*

Contact: Gretchen Ploen

Tel: 858-587-4404; Fax: 858-587-4438

E-Mail: Med.edu@scrippshealth.or

**20<sup>th</sup> Australasian Society for HIV Medicine Conference**

Sep 17-20, 2008

Perth, WA, *Australia*

Contact: Daliah Frank

Tel: 61-282-040-770; Fax: 61-292-124-670

E-Mail: conferenceinfo@ashm.org.au

**Peripheral T-Cell Lymphoma Forum**

Sep 18-20, 2008

Washington, DC, *United States*

Contact: Damaris Cruz

Tel: 201-594-0400; Fax: 201-594-0409

E-Mail: dcruz@jwoodassoc.com

**Management of Chronic Kidney Disease**

Sep 22-25, 2008

Coventry, England, *United Kingdom*

Contact: Dr Charlotte Moonan

Tel: 024-76-523-540; Fax: 024-76-523-701

E-Mail: Charlotte.Moonan@warwick.ac.uk



**6<sup>th</sup> World Stroke Congress**

Sep 24-27, 2008

Vienna, *Austria*

Contact: Ms. Rina Kinris

Tel: 41-229-080-488; Fax: 41-227-322-850

E-Mail: stroke2008@kenes.com

**Paediatric Gastroenterology Course**

Sep 25-27, 2008

Valletta, *Malta*

Contact: Dr. Chris Fearne

Tel: 00-35-679-707-209

E-Mail: christopher.fearne@gov.mt

**2008 Gastrointestinal Oncology Conference**

Sep 25-27, 2008

Arlington, VA, *United States*

Contact: Conference Secretariat: International Society of Gastrointestinal Oncology, Mr. Robert Ross, 200 Broadhollow RD, 11747 Melville

Tel: 1-631-390-8390; Fax: 1-631-393-5091

E-Mail: email@isgio.org

**European Conference on Paediatric Anaesthesia**

Sep 25-27, 2008

Athens, *Greece*

Contact: Aktina CityCongress S.A.

Tel: 302-103-232-433; Fax: 302-103-232-338

E-Mail: feapa2008@qaktinacitycongress.com

**6<sup>th</sup> Annual World Congress on Insulin Resistance Syndrome**

Sep 25-27, 2008

Los Angeles, CA, *United States*

Contact: Nava Mekel

Tel: 818-342-1889; Fax: 818-342-1538

E-Mail: insulinresistance@pacbell.net

**ISN Nexus symposium on Transplantation and the Kidney**

Sep 25-28, 2008

Rome, *Italy*

Contact: Michael Podt

E-Mail: michael.podt@isn-online.org

**6<sup>th</sup> Advanced Symposium on Congenital Heart Disease in the Adult**

Sep 26-27, 2008

Thessaloniki, *Greece*

Contact: Ms Artemis Thoma

Tel: 00-302-310-265-898; Fax: 00-302-310-240-669

E-Mail: thesis@thesis-pr.com

**Ophthalmic Anesthesia Society (OAS) 22<sup>nd</sup>**

Annual Meeting

Sep 26-28, 2008

Chicago, IL, *United States*

Contact: Karen S. MORGAN

Tel: 1-805-534-0300; Fax: 1-805-534-9030

E-Mail: info@eyeanesthesia.org

**13<sup>th</sup> International Congress on Hormonal Steroids and Hormones & Cancer**

Sep 27-30, 2008

Quebec City, QC, *Canada*

Contact: Secretariat

Tel: 418-654-2704; Fax: 418-654-2735

E-Mail: info@ichshc2008.com

**40<sup>th</sup> Congress of the International Society of Paediatric Oncology**

Oct 01-06, 2008

Berlin, *Germany*

Contact: Conference Secretariat: SIOP 2008

Secretariat, c/o MCI Berlin Office, Ines Paschen, Markgrafenstrasse 56, 10117 Berlin

Tel: 49-30-204-590; Fax: 49-302-045-950

E-Mail: siop2008@cpb.de

**4<sup>th</sup> World Congress on Quality in Medical Practice**

Oct 02-05, 2008

Thessaloniki, *Greece*

Contact: Psirropoulos Dimitrios Z, MD. PhD

Tel: 00-302-310-963-286; Fax: 00-302-310-963-288

E-Mail: cardio.gennim.thess@mail.gr

**Ultrasonography for Nephrologists**

Oct 03-05, 2008

Atlanta, GA, *United States*

Contact: Continuing Medical Education, 1462

Clifton Road, Suite 276 Atlanta, GA 30322

Tel: 1-888-727-5695 / 404-727-5695; Fax: 404-727-5667

E-Mail: cme@emory.edu

**2<sup>nd</sup> Mediterranean Clinical Immunology Meeting**

Oct 04-07, 2008

Antalya, *Turkey*

Contact: Mrs. Ayse Askin-Erten

Tel: 902-122-823-373; Fax: 902-122-823-321

E-Mail: immunology@serenas.com.tr

**Chest imaging 2008**

Oct 05-07, 2008

Boston, MA, *United States*

Contact: Harvard Medical School CME Office

Tel: 617-384-8600; Fax: 617-384-8686

E-Mail: hms-cme@hms.harvard.edu

National **Cancer Research** Institute Conference 2008  
Oct 05-08, 2008  
Birmingham, England, *United Kingdom*  
Contact: Conference Secretariat: NCRI Conference Secretariat Ms Sharon Vanloo, P.O. Box 49709 61 Lincoln's Inn Fields, WC2A 3 London  
Tel: 44-2-0-72-693-420; Fax: 44-2-0-70-616-004  
E-Mail: ncriconference@ncri.org.uk

5<sup>th</sup> World Congress of the European Club for **Paediatric Burns**  
Oct 08-11, 2008  
Gdansk, *Poland*  
Contact: Wyrzykowski Dariusz  
Tel: 48-601-685-379; Fax: 00-48-583-026-427  
E-Mail: pedsurg@amg.gda.pl

Acute Care **Psychiatry** Clinical Review  
Oct 09-11, 2008  
Chicago, IL, *United States*  
Contact: Vicki Klein  
Tel: 800-323-2688; Fax: 507-284-0532  
E-Mail: cme@mayo.edu

**Rheumatology & Cardiovascular** Medicine  
Oct 11-25, 2008  
Istanbul, *Turkey*  
Contact: Dr. Martin Gerretsen  
Tel: 1-888-647-7327; Fax: 1-888-547-7337  
E-Mail: cruises@seacourses.com

2008 **Cardiometabolic Health** Congress  
Oct 15-18, 2008  
Boston, MA, *United States*  
Contact: Dina Kouveliotis  
Tel: 877-571-4700; Fax: 866-218-9168  
E-Mail: dk@cardiometabolichealth.org

International Congress of **Pediatric Hepatology, Gastroenterology and Nutrition** (11th)  
Oct 15-18, 2008  
Sharm El-Sheikh, *Egypt*  
Contact: Professor Mortada El-Shabrawi, MD  
Tel: 20-123-133-705; Fax: 20-237-619-012  
E-Mail: melshabrawi@kasralainy.edu.eg

7<sup>th</sup> Annual Advances in **Breast MRI**  
Oct 16-18, 2008  
Las Vegas, NV, *United States*  
Contact: Stanford Radiology CME  
Tel: 650-473-5052; Fax: 650-473-5062  
E-Mail: radiologycme@med.stanford.edu

**Laser** Congress Korea 2008  
Oct 16-19, 2008  
Seoul, *Republic of Korea*  
Contact: Joung OK Lee MD  
Tel: 82-25-113-713; Fax: 82-25-173-713  
E-Mail: KHG000@UNITEL.CO.KR

8th Symposium on Advances in **Cardiac** Diseases  
Oct 17-18, 2008  
Turin, *Italy*  
Contact: Ms Barbara Rossi  
Tel: 39-0-10-583-224; Fax: 39-0-105-531-544  
E-Mail: acd2008@aristea.com

6<sup>th</sup> Australasian **Viral Hepatitis** Conference  
Oct 20-22, 2008  
Brisbane, QLD, *Australia*  
Contact: Nicole Robertson  
Tel: 61-282-040-770; Fax: 61-292-124-670  
E-Mail: conferenceinfo@hepatitis.org.au

XXIV National **Cardiology** Congress of the Turkish Society of Cardiology  
Oct 24-27, 2008  
Antalya, *Turkey*  
Contact: Meeting Organiser  
E-Mail: tkd@tkd.org.tr

Acute **Cardiac Care** 2008  
Oct 25-28, 2008  
Versailles, *France*  
Contact: Meeting Organiser  
E-Mail: EuroACCsecretariat@escardio.org

12<sup>th</sup> Biennial International **Gynecologic Cancer** Society Meeting  
Oct 25-28, 2008  
Bangkok, *Thailand*  
Contact: Conference Secretariat: International Gynecologic Cancer Society, PO Box 1726, CH-121 Geneva  
Tel: 41-229-080-488; Fax: 41-227-322-850  
E-Mail: igcs-11@kenes.com

5<sup>th</sup> French-Brazilian **Oncology** Congress  
Nov 06-08, 2008  
Rio De Janeiro, *Brazil*  
Contact: Conference Secretariat: Sociedade Franco Brasileira de Oncologia c/o Successevents, carla Ismael, Avenida Nossa Senhora de Copacabana 1059/601, 22060- Rio de Janeiro  
Tel: 55-212-247-7874; Fax: 55-212-247-7874  
E-Mail: Vcongresso@sbo.com.br

American College of **Allergy, Asthma & Immunology** Annual Meeting 2009  
Nov 06-11, 2009  
Miami Beach, FL, *United States*  
Contact: Meeting Organiser  
Tel: 847-427-1294; Fax: 847-427-1200  
E-Mail: mail@acaai.org / meetings@acaai.org

# WHO-Facts Sheet

1. Monitoring AIDS Treatment by Physical Symptoms is Effective
2. The Impact of Climate Change on Human Health
3. Climate Change will Erode the Foundations of Health
4. WHO Reports Highest Rates of Drug-Resistant Tuberculosis To Date
5. Monitoring AIDS Treatment by Regular Physical Examination is Nearly as Effective as Advanced Laboratory Tests

Compiled and edited by  
Babichan K Chandy

Kuwait Medical Journal 2008, 40 (2): 175-180

## 1. MONITORING AIDS TREATMENT BY PHYSICAL SYMPTOMS IS EFFECTIVE

### Result is almost as good as therapies based on advanced laboratory tests, a new study finds

When millions of HIV-infected people in poor countries began receiving advanced drug therapies, critics worried that patient care would suffer because few high-tech laboratories were available to guide treatments. But according to a study being published in *The Lancet*, these concerns are as yet unfounded. In fact, the study indicates that when clinicians use simple physical signs of deteriorating health -- such as weight loss or fever -- these doctors can provide therapies almost as effective as those relying on the most advanced laboratory analysis.

"The results of this study should reassure clinicians in Africa and Asia, who are treating literally millions of people without these laboratory tests, that they are not compromising patient safety," said a coauthor of the paper, Dr Charles Gilks, who is the Coordinator of Antiretroviral Treatment (ART) and HIV Care at WHO in Geneva. "In fact, the outcome of their treatment is almost as good as of those patients in the USA and Europe where laboratory-guided treatment is the norm."

The aim of the study was to look at the medium and long-term consequences of different approaches to monitoring antiretroviral therapy in a resource-limited setting: using clinical signs and symptoms alone as recommended in WHO guidelines; or more sophisticated and costly but far less accessible immunological and virological load tests. The scientists used a model that had been tried and tested in London, and shown accurately to predict the course of the epidemic in the UK over 20 years, but with various changes to reflect realities on the ground.

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According to the study authors, survival rates for individuals assessed for clinical symptoms alone were almost identical to survival rates for those who underwent laboratory monitoring. The 5-year survival rate was 83% for individuals monitored for viral load, 82% for CD4 (a critical immune component) monitoring, and 82% for clinical monitoring alone. Corresponding values over a 24-year period were 67%, 64% and 64% respectively.

Although the survival rate was slightly higher with viral load monitoring, study authors pointed out it was not the most cost-effective strategy in the poorest countries. The study also examined whether clinical observation alone was effective in determining when to switch patients from WHO-recommended first-line treatments to more costly second-line medicines. Again, diagnosis based on an assessment of clinical symptoms was almost as effective as those relying on expensive laboratory tests.

Study authors concluded that for patients on the WHO first-line regimen of stavudine, lamivudine and nevirapine, the benefits of CD4 count or viral load monitoring were only modest at best.

The study, conducted by a prominent group in the United Kingdom working with WHO scientists, employed mathematical models which were designed to identify emerging problems and problems that might appear after long-term use of ART. But more work must be done. The study is based on mathematical projections and not on real-world patients. While there is little real-world data yet available because these drugs have been used for such a short time in these countries, the little existing information does support the findings. Other studies are ongoing and more results should be available soon.

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## 2. THE IMPACT OF CLIMATE CHANGE ON HUMAN HEALTH

### A Statement by the World Health Organization Director-General

Last year marked a turning point in the debate on climate change. The scientific evidence continues to mount. The climate is changing, the effects are already being felt, and human activities are a principal cause.

In selecting climate change as the theme for this year's World Health Day, WHO aims to turn the attention of policy-makers to some compelling evidence from the health sector. While the reality of climate change can no longer be doubted, the magnitude of consequences, and -- most especially for health -- can still be reduced. Consideration of the health impact of climate change can help political leaders move with appropriate urgency.

The core concern is succinctly stated: climate change endangers health in fundamental ways. The warming of the planet will be gradual, but the effects of extreme weather events -- more storms, floods, droughts and heatwaves -- will be abrupt and acutely felt. Both trends can affect some of the most fundamental determinants of health: air, water, food, shelter, and freedom from disease.

Although climate change is a global phenomenon, its consequences will not be evenly distributed. Scientists agree that developing countries and small island nations will be the first and hardest hit.

#### WHO has identified five major health consequences of climate change:

**First**, the agricultural sector is extremely sensitive to climate variability. Rising temperatures and more frequent droughts and floods can compromise food security. Increases in malnutrition are expected to be especially severe in countries where large populations depend on rain-fed subsistence farming. Malnutrition, much of it caused by periodic droughts, is already responsible for an estimated 3.5 million deaths each year.

**Second**, more frequent extreme weather events mean more potential deaths and injuries caused by storms and floods. In addition, flooding can be followed by outbreaks of diseases, such as cholera, especially when water and sanitation services

are damaged or destroyed. Storms and floods are already among the most frequent and deadly forms of natural disasters.

**Third**, both scarcities of water, which is essential for hygiene, and excess water due to more frequent and torrential rainfall will increase the burden of diarrhoeal disease, which is spread through contaminated food and water. Diarrhoeal disease is already the second leading infectious cause of childhood mortality and accounts for a total of approximately 1.8 million deaths each year.

**Fourth**, heatwaves, especially in urban "heat islands", can directly increase morbidity and mortality, mainly in elderly people with cardiovascular or respiratory disease. Apart from heatwaves, higher temperatures can increase ground-level ozone and hasten the onset of the pollen season, contributing to asthma attacks.

**Finally**, changing temperatures and patterns of rainfall are expected to alter the geographical distribution of insect vectors that spread infectious diseases. Of these diseases, malaria and dengue are of greatest public health concern.

In short, climate change can affect problems that are already huge, largely concentrated in the developing world, and difficult to combat.

Only, better systems for surveillance and forecasting, and stronger basic health services, can offer health protection. Citizens, too, need to be fully informed of the health issues. In the end, it is their concerns that can spur policy-makers to take the right actions, urgently.

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## 3. CLIMATE CHANGE WILL ERODE THE FOUNDATIONS OF HEALTH

### WHO Director-General warns vulnerable populations at greatest risk of projected impacts

Scientists tell us that the evidence the Earth is warming is "unequivocal." Increases in global average air and sea temperature, ice melting and rising global sea levels all help us understand and prepare for the coming challenges. In addition to these observed changes, climate-sensitive impacts on human health are occurring today. They are attacking the pillars of public health. And they are providing a glimpse of the challenges public health will have to confront on a large scale, Dr Margaret Chan, Director-General of the World Health Organization (WHO), warned on the occasion of World Health Day<sup>[1]</sup>.



"The core concern is succinctly stated: climate change endangers human health," said Dr Chan. "The warming of the planet will be gradual, but the effects of extreme weather events -- more storms, floods, droughts and heatwaves -- will be abrupt and acutely felt. Both trends can affect some of the most fundamental determinants of health: air, water, food, shelter and freedom from disease".

Human beings are already exposed to the effects of climate-sensitive diseases and these diseases today kill millions. They include malnutrition, which causes over 3.5 million deaths per year, diarrhoeal diseases, which kill over 1.8 million, and malaria, which kills almost 1 million.

**Examples** already provide us with images of the future:

- **European heat wave 2003:** Estimates suggest that approximately 70,000 more people died in that summer than would have been expected.
- **Rift Valley Fever in Africa:** Major outbreaks are usually associated with rains, which are expected to become more frequent as the climate changes.
- **Hurricane Katrina, 2005:** Over 1800 died and thousands more were displaced. Additionally, health facilities throughout the region were destroyed critically affecting health infrastructure.
- **Malaria in the East African Highlands:** In the last 30 years, warmer temperatures have also created more favourable conditions for mosquito populations in the region and therefore for transmission of malaria.
- **Epidemics of cholera in Bangladesh:** They are closely linked to flooding and unsafe water.

These trends and events cannot be attributed solely to climate change but they are the types of challenges we expect to become more frequent and intense with climate changes. They will further strain health resources which, in many regions, are already under severe stress.

"Although climate change is a global phenomenon, its consequences will not be evenly distributed," said Dr Chan. "In short, climate change can affect problems that are already huge, largely concentrated in the developing world, and difficult to control."

To address the health effects of climate change, WHO is coordinating and supporting research and assessment on the most effective measures to protect health from climate change, particularly for vulnerable populations such as women and children in developing countries, and is advising Member States on the necessary adaptive changes to their health systems to protect their populations.

WHO and its partners -- including the UN Environment Programme, the Food and Agriculture

Organization, and the UN World Meteorological Organization -- are devising a workplan and research agenda to get better estimates of the scale and nature of health vulnerability and to identify strategies and tools for health protection. WHO recognizes the urgent need to support countries in devising ways to cope. Better systems for surveillance and forecasting, and stronger basic health services, can offer health protection. WHO will be working closely with its Member States in coming years to develop effective means of adapting to a changing climate and reducing its effects on human health.

"Through its own actions and its support to Member States," said Dr Chan, "WHO is committed to do everything it can to ensure all is done to protect human health from climate change."

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#### 4. WHO REPORTS HIGHEST RATES OF DRUG-RESISTANT TUBERCULOSIS TO DATE

Multidrug-resistant tuberculosis (MDR-TB) has been recorded at the highest rates ever, according to a new World Health Organization (WHO) report that presents findings from the largest survey to date on the scale of drug resistance in tuberculosis.

The report, *Anti-Tuberculosis Drug Resistance in the World*, is based on information collected between 2002 and 2006 on 90,000 TB patients in 81 countries. It also found that extensively drug-resistant tuberculosis (XDR-TB), a virtually untreatable form of the respiratory disease, has been recorded in 45 countries.

The report also found a link between HIV infection and MDR-TB. Surveys in Latvia and Donetsk, Ukraine found nearly twice the level of MDR-TB among TB patients living with HIV compared with TB patients without HIV.

Based on analysis of the survey data, WHO estimates there are nearly half a million new cases of MDR-TB--about 5% of the total nine million new TB cases--worldwide each year. The highest rate was recorded in Baku, the capital of Azerbaijan, where nearly a quarter of all new TB cases (22.3%) were reported as multidrug-resistant. Proportions of MDR-TB among new TB cases were 19.4% in Moldova, 16% in Donetsk in Ukraine, 15% in Tomsk Oblast in the Russian Federation and 14.8%

in Tashkent in Uzbekistan. These rates surpass the highest levels of drug resistance published in the last WHO report in 2004. Surveys in China also suggest that MDR-TB is widespread in that country.

"TB drug resistance needs a frontal assault. If countries and the international community fail to address it aggressively now we will lose this battle," said Dr Mario Raviglione, Director of the WHO Stop TB Department. "In addition to specifically confronting drug-resistant TB and saving lives, programmes world-wide must immediately improve their performance in diagnosing all TB cases rapidly and treating them until cured, which is the best way to prevent the development of drug resistance."

For the first time, the global survey includes analysis of XDR-TB. However, because few countries are equipped at present to diagnose it, limited data were available for this report.

Although the report highlights the extent of drug resistance, it also points to some successes. Thirteen years ago, Estonia and Latvia were singled out by WHO as drug-resistant TB "hotspots". Today, following a substantial investment and a sustained assault on MDR-TB, rates in these two Baltic countries are stabilizing and TB case notification rates are falling.

The true scale of the problem also remains unknown in some pockets of the world. Only six countries in Africa—the region with the highest incidence of TB in the world\*\*\*--were able to provide drug resistance data for the report. Other countries in the region could not conduct surveys because they lack the equipment and trained personnel needed to identify drug-resistant TB. "Without these data, it is difficult to estimate the true burden and trends of MDR-TB and XDR-TB in the region. It is likely there are outbreaks of drug resistance going unnoticed and undetected," said WHO TB expert Abigail Wright, the principal author of the report.

WHO estimates that US\$4.8 billion is needed for overall TB control in low- and middle-income countries in 2008, with US\$1 billion for MDR-TB and XDR-TB. But there is a total financing gap of \$2.5 billion, including a US\$ 500 million gap for MDR-TB and XDR-TB.

"The threat created by TB drug resistance demands that we fill these gaps, as laid out in the Global Plan to Stop TB, a roadmap for halving TB prevalence and deaths compared with 1990 levels by 2015," said Dr Marcos Espinal, Executive Secretary of the Stop TB Partnership. "The Plan also calls for another imperative--sufficient resources for research to find new diagnostics, new drugs effective against resistant strains and an effective TB vaccine."

### Important Note:

\* The bacteria responsible for TB become resistant when people ill with TB are not provided with or do not complete a full course of medication. Drug-resistant TB, like drug-sensitive TB, can also be transmitted through the air from an infected person to a non-infected person. MDR-TB is a form of TB that does not respond to the standard six month treatment using first line-drugs (i.e. resistant to isoniazid and rifampicin). It can take two years to treat with drugs that are 100 times more expensive than first-line treatment.

\*\* XDR-TB is a form of TB caused by bacteria resistant to virtually all the most effective anti-TB drugs (i.e. MDR-TB plus resistance to any fluoroquinolones and any one of the second-line anti-TB injectable drugs: amikacin, kanamycin or capreomycin).

\*\*\* In sub-Saharan Africa HIV / AIDS is dramatically fuelling the spread of TB. TB is a major cause of death among people living with HIV. MDR-TB and XDR-TB are highly lethal in people living with HIV -- studies show case fatality rates of over 90%. Drug-resistant TB is therefore a major threat to the effectiveness of both TB treatment and anti-retroviral treatment programs.

### Worldwide Efforts to Confront Tuberculosis are Making Progress, but Too Slowly:

The World Health Organization (WHO) report, *Global Tuberculosis Control 2008*, released in March 2008, finds that the pace of the progress to control the tuberculosis (TB) epidemic slowed slightly in 2006, the most recent year for which data were available. The new information documents a slowdown in progress on diagnosing people with TB. Between 2001 to 2005, the average rate at which new TB cases were detected was increasing by 6% per year; but between 2005 and 2006 that rate of increase was cut in half, to 3%.

The reason for this slowing of progress is that some national programmes that were making rapid strides during the last five years have been unable to continue at the same pace in 2006. Moreover, in most African countries there has been no increase in the detection of TB cases through national programmes. Other studies have also shown that many patients are treated by private care providers, and by non-governmental, faith-based and community organizations, thus escaping detection by the public programmes.

"We've entered a new era," said Dr Margaret Chan, WHO Director-General. "To make progress, firstly public programmes must be further strengthened. Secondly, we need to fully tap the potential of other service providers. Enlisting

these other providers, working in partnership with national programmes, will markedly increase diagnosis and treatment for people in need". The twelfth annual WHO report on global TB control, is based on data given to WHO by 202 countries and territories.

There were 9.2 million new cases of TB in 2006, including 700,000 cases among people living with HIV, and 500,000 cases of multi-drug resistant TB (MDR-TB). An estimated 1.5 million people died from TB in 2006. In addition, another 200,000 people with HIV died from HIV-associated TB.

The report highlighted two aspects of the epidemic that could further slow progress on TB. The first is multidrug-resistant tuberculosis (MDR-TB), reported by WHO last month to have reached the highest levels ever recorded. To date, however, the response to this epidemic has been inadequate. Given limited laboratory and treatment capacity, countries project they will provide treatment only to an estimated 10% of people with MDR-TB worldwide in 2008.

The second threat to continued progress is the lethal combination of TB and HIV, which is fuelling the TB epidemic in many parts of the world, especially Africa. Although TB/HIV remains a massive challenge, some countries are making strides against the co-epidemic. Almost 700 000 TB patients were tested for HIV in 2006, up from 22 000 in 2002--a sign of progress but still far from the 2006 target of 1.6 million set by the Global Plan to Stop TB 2006-2015.

"The report tells us that we are far from providing universal access to high-quality prevention, diagnostic, treatment and care services for HIV and TB," said Dr Peter Piot, Executive Director of UNAIDS. "Clear progress has been made but we must all do more to make a joint approach to reducing TB deaths among people with HIV a reality."

The report also documents a shortage in funding. Despite an increase in resources, especially from the Global Fund and some middle-income countries, TB budgets are projected to remain flat in 2008 in almost all of the countries most heavily burdened by the disease. Ninety countries in which 91% of the world's TB cases occur provided complete financial data for the Report. To meet the 2008 targets of the Global Plan to Stop TB, the funding shortfall for these 90 countries is about US\$ 1 billion.

"We look forward to working with all partners to further assist countries to achieve TB targets for 2015 and beyond," said Dr Michel Kazatchkine, Executive Director of the Global Fund to Fight AIDS, Tuberculosis and Malaria. "Together we are bringing hope to the individuals and communities suffering from the enormous burden of TB."

In recognition of World TB Day, Dr Jorge Sampaio, former President of Portugal and the UN Secretary-General's Special Envoy to Stop TB, called for enhanced leadership to address TB/HIV. "TB is a leading cause of death among people living with HIV/AIDS," he said. "Several countries have shown that targets relating to TB/HIV are achievable and have put in place measures that will have an impact on the lives of those at most risk. But this is a restless battle. We still need to do much more and much better."

**Change in WHO classification of causes of death:** This year, under new guidelines, deaths from a combination of HIV and TB are no longer classified as TB deaths.

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#### **5. MONITORING AIDS TREATMENT BY REGULAR PHYSICAL EXAMINATION IS NEARLY AS EFFECTIVE AS ADVANCED LABORATORY TESTS**

When millions of HIV-infected people in poor countries began receiving advanced drug therapies, critics worried that patient care would suffer because few high tech laboratories were available to guide treatments. But according to a study being published in Lancet Friday, 25 April, these concerns are as yet unfounded. In fact, the study indicates that when clinicians use simple physical signs of deteriorating health -- such as weight loss or fever -- these doctors can provide therapies almost as effective those relying on the most advanced laboratory analysis.

"The results of this study should reassure clinicians in Africa and Asia, who are treating literally millions of people without these laboratory tests, that they are not compromising patient safety," said a coauthor of the paper, Dr Charles Gilks, the Coordinator of Antiretroviral Treatment (ART) and HIV Care at the World Health Organization in Geneva. "In fact, the outcome of their treatment is almost as good as those patients in the USA and Europe where laboratory-guided treatment is the norm."

The aim of the study was to look at the medium and long-term consequences of different approaches to monitoring antiretroviral therapy in a resource limited setting: using clinical signs and symptoms alone as recommended in WHO guidelines; or more sophisticated and costly but far less accessible

immunological and virological load tests. The scientists used a model that had been tried and tested in London, and shown accurately to predict the course of the epidemic in the UK over twenty years, but with various changes to reflect realities on the ground.

According to the study authors, survival rates for individuals assessed for clinical symptoms alone were almost identical to those who underwent laboratory monitoring. The 5-year survival rate was 83% for individuals monitored for viral load, 82% for CD4 (a critical immune component) monitoring, and 82% for clinical monitoring alone. Corresponding values over a 24-year period were 67%, 64% and 64% respectively.

Although the survival rate was slightly higher with viral load monitoring, study authors pointed out it was not the most cost-effective strategy in the poorest countries. The study also examined whether clinical observation alone was effective in determining when to switch patients from WHO-recommended first-line treatments to more costly second-line medicines. Again, diagnosis based on an assessment of clinical symptoms was almost as effective as those relying on expensive laboratory tests.

Study authors concluded that, for patients on the WHO first-line regimen of stavudine, lamivudine and nevirapine, the benefits of CD4 count or viral load monitoring were only modest at best.

The study, by a prominent group in the United Kingdom working with WHO scientists, employs mathematical models which were designed to identify emerging problems and problems that might appear after long term use of ART. But more work must be done. The study is based on mathematical projections and not on real world patients. While there is little real world data yet available, because these drugs have been used for such a short time in these countries, the little existing information does support the findings. Other studies are ongoing and more results should be available soon.

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