

## Determination of fundal height increase in fasting and non-fasting pregnant women during Ramadan

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**F**asting, preventing of taking food and drink from the breaking of dawn to the setting of sun, is a specific religious practice that is obligatory to Muslims based on their actual physical capabilities. Old people, sick people, travelers in certain conditions, pregnant and nursing women when either their own or their fetus/neonate's health is in danger are exempted from fasting, but must make it up as they are able.<sup>1</sup> It has been observed that fasting during pregnancy has no harmful effect on the mother and her fetus, but still some pregnant women prevent from fasting because of the fear of probable harmful effects, while some others insist on fasting even in risky cases due to religious fanaticism. In taking any decision during pregnancy, the health of both mother and her fetus should be considered. In previous studies the effects of fasting on breast feeding and neonate birth weight,<sup>2</sup> premature labor,<sup>3</sup> metabolic changes and clinical symptoms before breakfast (Iftar)<sup>4</sup> have been investigated and no harmful effect has been observed in these cases. The aim of this case-control study was to investigate the effects of fasting on intrauterine growth by comparing 2 groups of fasting and non-fasting pregnant women (20-31 weeks) and also comparing the rate of growth in Ramadan with that in the preceding and following months.

One of the basic and reliable criterions for the evaluation of intrauterine growth is the serial measuring of fundal height at the monthly prenatal check-up.<sup>5</sup> According to some researchers, fundal height in centimeters is equal to the weeks of gestation until the 34th week.<sup>5</sup> In other words, up to the 34th week, fundal height increase obeys an arithmetical progression that is a 4 cm increase monthly.

This case-control study was carried out on 101 pregnant women at the gestational age of 18th-28th weeks referred to Kerman private prenatal care clinics in 2001. Two groups were selected and matched for age, socio-economic status and previous delivery complications. The case group consisted of 51 pregnant women who fasted at least 20 days during Ramadan and control group consisted of 50 non-fasting pregnant women. All subjects had 5 serial examinations every 4 weeks. Examinations were performed one month before Ramadan, at the beginning of Ramadan, at the end of Ramadan, one and 2 months after Ramadan. The

results of examinations including mother's weight, blood pressure and fundal height were recorded. At the end of Ramadan gestational age (based on biparietal diameter and femur length) and amniotic fluid volume (based on vertical diameter of amniotic pocket) were determined by sonography and recorded. After delivery neonate birth weight as well as other demographic features were recorded. Data analysis was carried out with the Statistical Package for Social Sciences and by using t-test, correlation and descriptive statistics. Among the 101 studied women, 51 women fasted for at least 20 days in Ramadan of which 7 women also fasted the first 10 days of Rajab and 3 women fasted the first 10 days of Shaban as well. The mean age of the case group was  $28.29 \pm 5.48$  and that of the control group was  $28.78 \pm 5.7$ . Mean of gravity in the fasting group was  $2.65 \pm 1.51$  and  $3.04 \pm 1.70$  in the non-fasting group. There was no significant difference between the 2 groups in regard to age ( $p=0.592$ ) and gravity ( $p=0.354$ ). In 33 women from the fasting group the mean neonate birth weight in previous pregnancy was  $3.31 \pm 0.354$  and in 34 women of the non-fasting group the mean birth weight of previous pregnancy was  $3.40 \pm 0.543$  showing no significant difference between the 2 groups in this regard ( $p=0.721$ ). There was no significant difference between the 2 groups in the mean weight of mothers at the beginning and end of Ramadan. Mothers' weight increased during the 4 months of study and showed no significant difference in the 2 groups. There was also no significant difference between the case and control groups in fundal height increase in the 5 performed examinations ( $p=0.258, 0.201, 0.191, 0.208$  and  $0.120$ ) and the rate of fundal height increase during the 4 months of study was almost the same in the 2 groups. In regard to the blood pressure, there was no significant difference between the 2 groups in systolic blood pressure in any of the examinations, but diastolic blood pressure in the first and last examinations was significantly different in the 2 groups ( $p<0.009$  and  $p<0.017$ ). At the end of Ramadan there was no significant difference between case and control groups in gestational age determined based on last menstrual period (LMP), fundal height and sonography report. In the fasting group gestational age determined based on LMP, fundal height and sonography were the same but in the control group gestational age determined by LMP was lower than that estimated by fundal height and sonography. No significant difference was observed between the 2 groups in gestational age and amniotic fluid volume reported by sonography at the end of Ramadan. Mean birth weight was  $3.289 \pm 0.348$  and  $3.325 \pm 0.337$  in the case and control groups, showing no significant difference ( $p=0.999$ ). There was also no significant difference

between the current birth weight and previous birth weight in both groups.

The results of the present study conducted on 51 fasting and 50 non-fasting pregnant women, show no significant difference between the 2 groups in regard to mothers' weight increase, fundal height, amniotic fluid volume and neonates' birth weight. Mothers' blood pressure, weight and all parameters determined by sonography showed no significant difference in the 2 groups. As subjects in the 2 groups were matched for age, weight, parity and socio-economic status and all have a similar ordinary diet, it can be concluded that in healthy mothers, Islamic fasting has no harmful effect on intrauterine growth and neonate's birth weight.

Received 21st October 2003. Accepted for publication in final form 10th February 2004.

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Achromobacter xylosoxidans isolated from the sputum of a patient with cystic fibrosis mutation I1234V with *Pseudomonas aeruginosa*

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Chronic bacterial pulmonary infections are a major cause of morbidity and mortality in patients with cystic fibrosis (CF).<sup>1</sup> The causative organisms are commonly *Pseudomonas aeruginosa* (*P. aeruginosa*), *Staphylococcus aureus* and *Haemophilus influenzae* but unusual pathogens and antibiotic-resistance organisms such as mucoid *P.*

*aeruginosa*, *Burkholderia cepacia*, *Stenotrophomonas maltophilia* and *Achromobacter xylosoxidans* (*A. xylosoxidans*) are being recovered increasingly from patients with more advanced CF disease.<sup>2</sup> *Achromobacter xylosoxidans*, a motile gram-negative, oxidase-positive rod is present in aquatic environments and in the normal human gastrointestinal flora. In 1971 it was classified as *Achromobacter*, was redesignated *Alcaligenes* in 1984 and was reclassified *Achromobacter* in 1998. It causes infection in the immuno-compromised patient, meningitis in newborn infants, peritonitis in patients receiving peritoneal dialysis and contact lens-keratitis and has been isolated from the respiratory tract of non-CF patients on long-term mechanical ventilation.<sup>3</sup> It may contaminate hospital equipment and fluids and can lead to nosocomial outbreaks of infection. The role of *A. xylosoxidans* in accelerating the decline of lung function in CF patients is questionable, as several reports have found no strong association between chronic *A. xylosoxidans* infection and deterioration in lung function.<sup>4</sup>

*Achromobacter xylosoxidans*, sensitive to cefepime and amikacin, was isolated recently from the sputum of a 16-year-old Arab Qatari male with CF carrying the pathogenic mutation I1234V of the CF transmembrane conductance regulator and previously diagnosed with chronic endobronchial colonization with *P. aeruginosa* for 6 years. After receiving cefepime and amikacin intravenously for 3 weeks, his clinical condition and his pulmonary function test both improved although, while remaining clinically stable, sputum cultures over 6 months repeatedly produced persistent growths of *A. xylosoxidans* in addition to mucoid and non-mucoid *P. aeruginosa*. It is suggested that the presence of unusual pathogens and antibiotic-resistant organisms, co-existing with chronic *P. aeruginosa* infection could contribute to clinical deterioration in such patients during pulmonary exacerbation. Patients with CF are now surviving to a median age of 32.3 years and those 18 years old or older now constitute one-third of the total population.<sup>4</sup> Intensive use of antibiotics theoretically increases the likelihood of opportunistic infections with inherently resistant organisms.<sup>2</sup> The clinical significance of *A. xylosoxidans* in CF is not clear although some clinicians believe it adds to patient morbidity. It is capable of causing persistent infection or colonization of the respiratory tract of patients with CF,<sup>3</sup> is found in approximately 9% of these patients, and is frequently confused with species in the *Burkholderia cepacia* complex. Accurate identification of these antibiotic-resistant gram-negative bacteria is critical for proper treatment and infection control. One clinical study suggested that CF pulmonary exacerbation might be

associated with *A. xylosoxidans* but it was difficult to determine the significance of this link because of the concomitant isolation of *P. aeruginosa* infection.<sup>3</sup> *Achromobacter xylosoxidans* species show multiple antibiotic resistance, especially to aminoglycosides, and variable sensitivity to third-generation cephalosporins.<sup>5</sup> As the life span of CF patients is increasing it is important to ascertain whether the organisms cultured from CF sputum are true pathogens or not. Individuals who harbor *A. xylosoxidans* infection do not appear to be a danger to other patients. This case suggests that *A. xylosoxidans* may contribute to clinical deterioration in patients with CF during pulmonary exacerbation, however the effect of chronic colonization of airways with *A. xylosoxidans* in the decline of lung function in CF is unclear.

Received 8th December 2003. Accepted for publication in final form 10th February 2004.

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Columnar lined esophagus. An attempt to find a useful definition and reproducible histopathological diagnostic criteria

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**B**arrett's esophagus (now better called columnar lined esophagus or CLO) was first described in 1950 by a British and London based Consultant Surgeon who referred to the disease bearing his name, as a form of chronic peptic ulcer and inflammation of the esophagus which is also

associated with the presence of columnar epithelium in the esophageal distal portion. Since then, not a single reliable definition of CLO was found. Both macroscopic and microscopic definitions do, however, exist each proposed in an effort to deal with diagnostic problems encountered in this disease. The association between CLO, dysplasia and adenocarcinoma was established by many investigators in the period between 1960 and 1970. In addition, the classification and the diagnostic histopathological criteria of the disease remain difficult and controversial. It is my intention, in this brief communication; to present suitable or at least logic definitions for CLO in addition to outlining the most recognized and recommended diagnostic features.

Classical or long segment CLO (LSCLO) has been defined as more than 3 cm of columnar-lined mucosa in the lower esophagus. "This 3cm rule" was later modified to lengths between 2 and 5cm being required for the diagnosis. The term short (SSCLO) and ultra short (USSCLO) segments diseases are hence reserved for lesions less than 2 cm in length. Ultra short segment CLO causes controversy because of the recent increasing evidence that the disease does not share the same etiological, pathogenetic and probably prognostic features of the other forms of CLO. It is also important to mention that SSCLO can be associated with intestinal metaplasia and in such cases, it can predispose to esophageal adenocarcinoma.

Most authorities believe that current dilemmas in the definition and diagnosis of CLO are caused by the following factors: 1. The presence of a natural variation of up to 2 cm between the histological squamo-columnar junction (SCJ) and the anatomical gastroesophageal junction (GOJ). 2. The location of SCJ and GOJ can change during peristalsis and inspiration, making measurements of LSCLO inherently inaccurate. If the length of acquired LSCLO cannot be measured with reasonable precision, there is a risk of over diagnosis. 3. While there is now considerable evidence that intestinal metaplasia (IM) is a critical component in the neoplastic process that complicates CLO and despite the fact that many workers have sought to define the disease by the presence of IM, it is obvious that relying on the demonstration of IM to define CLO is a risky strategy as demonstration of IM is dependent on the number and size of biopsies taken. It is, hence, clear that a strategy of relying solely on the demonstration of IM to define and diagnose CLO will result in considerable under diagnosis. 4. Presence of hiatus hernia, which, if "subtle" may not be even noticed by the endoscopist. Based on the above, we strongly believe, as many British authors do,<sup>1</sup> that it would

be logical to reject the subdivision of CLO into long and short segment provided that the length of CLO is specified and the presence and amount of IM is mentioned. This will, of course require a good number of biopsies (at least 8).

Recently, the British Society of Gastroenterology recommended the following histopathological criteria for the diagnosis of CLO:<sup>1</sup> 1. Biopsies diagnostic of CLO should have native esophageal structures (such as submucosal esophageal glands and their ducts) with juxtaposition to glandular mucosa. Such cases represent the one and only situation where the diagnostic histopathologist can make the diagnosis of CLO even without adequate clinical and endoscopic information. It is, however, fair to say that native esophageal glands are usually deeply seated in the submucosal layer and may be difficult to visualize in superficial and small biopsies. 2. Biopsies corroborative (confirmatory) of an endoscopic diagnosis of CLO should have intestinalized metaplastic glandular mucosa with or without non-organized arrangement, villous architecture, and patchwork of different glandular types. This pattern could, however, still be seen in incomplete intestinal metaplasia of stomach especially when associated with hiatus hernia or USSCLO. 3. Biopsies in keeping with but not specific for CLO: This category shows gastric type mucosa without intestinal metaplasia. The gastric glands show non-organized arrangement with patchwork appearance. This pattern could yet represent the normal gastroesophageal junction or the stomach with or without hiatus hernia. 4. Biopsies without evidence of CLO: The biopsies included in this category usually show esophageal type squamous epithelium with no evidence of glandular epithelium. Esophageal squamous epithelium showing basal cell hyperplasia, lengthening of the papillae with intraepithelial eosinophils and polymorphs is consistent however, with reflux esophagitis.

In addition to the above, it would be useful to mention the promising role of immunohistochemistry (cytokeratin 7 and 20) in distinguishing between intestinal metaplasia in CLO and IM that occurs in gastric mucosa.<sup>2-4</sup> In CLO, cytokeratin 7 stains the superficial and deep intestinalized mucosa while cytokeratin 20 shows only superficial band like staining of the metaplastic epithelium and it is claimed that this pattern of cytokeratin 7 and 20 immunoreactivity is unique to and characteristic of CLO and is not seen in intestinal metaplasia of gastric mucosa. However, other investigators have found discrepant results with these stains.<sup>5</sup>

We, like other pathologists recommend that diagnosis of CLO is made by endoscopy and confirmed by histopathological diagnosis. Essential

information for the diagnostic pathologist includes the length of CLO, the presence or absence of hiatus hernia and sites from which biopsies were taken. The reporting strategy which is currently introduced by the British Society of Gastroenterology<sup>1</sup> should aid the practicing histopathologist in the diagnosis of CLO as only occasionally are esophageal biopsies diagnostic for this disorder. Finally, it is advised to accept that CLO is better defined as the replacement of lower esophageal squamous mucosa by metaplastic glandular epithelium as a result of gastroesophageal reflux disease (GORD).

Received 31st August 2003. Accepted for publication in final form 10th January 2004.

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Fever due to malaria in a neutropenic patient. *A rare complication of blood transfusion*

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**I**nfection is a major cause of morbidity and mortality among patients with cancer, despite recent advances in its prevention and treatment. The incidence of infection increases significantly with prolonged duration of hospitalization, the degree of neutropenia and the use of glucocorticoids. In addition, cellular and humoral immune dysfunction and splenectomy can also predispose cancer patients

to certain types of infection. The majority of bacterial infections in patients with cancer result from the patients' own flora.<sup>1</sup> Infection by *Plasmodium vivax* (*P.vivax*) is rarely the cause of fever in a neutropenic patient. However, it is one of the leading diseases in the differential diagnosis of neutropenic fever, particularly in endemic parts of the world and it is one of the most important transfusion-associated parasites, especially in this area. We report neutropenic fever due to transfusion-related *P.vivax* infection in a patient with acute myeloblastic leukemia (AML-M2).

A 21-year-old man was admitted to our department in February 2002 with diagnosis of AML-M2. The patient was treated with standard induction and postremission regimen and complete remission was obtained and sustained until February 2003. Standard remission induction regimen was used again, and a second remission obtained. The patient was treated with high dose cytarabine (3 gr/m<sup>2</sup>, intravenously, 6 doses for 3 sequential days) for consolidation 10 days before admission. The patient was admitted, in May 2003 due to fever of 39.5°C, rigor and grade 4 neutropenia. The fever was intermittent, especially at morning and sustained at 4 hours. The leukocyte count was 0.4 x 10<sup>9</sup>/L and neutrophil count was 0.1x10<sup>9</sup>/L. Hemoglobin level was 9 gr/dl and platelet count 95.000/mm<sup>3</sup>. Due to neutropenic fever, empirical meropenem was initiated as soon as blood culture was taken. The fever did not respond to empirical meropenem within 48 hours of therapy. No microorganism was isolated from blood culture. Microscopical examination of Giemsa-stained blood film showed a mature trophozoite and a lot of infected red cells with plasmodium. *Plasmodium vivax* was confirmed with thick blood film. Chloroquine followed by Primaquine was started. The fever dropped within 30 hours. He has a history of multiple transfusions of blood and blood products from voluntary donors, but none of them had been screened for malaria. He was from a non-endemic area for plasmodium and no history of travel to other sites within Turkey or abroad, and no history of previous malaria episodes. However, primary or transfusion related malaria could not be distinguished clearly, and we suspected that he had been infected via blood transfusion.

Malaria infection is a protozoal disease transmitted from human to human by the bite of infected *Anopheles* mosquitoes. Congenital transmission and transmission by blood transfusion have also been reported. Malaria has now been eradicated in North America, Europe, and Russia. *Plasmodium falciparum* predominates in Africa, New Guinea, and Haiti; *P.vivax* is more common in Central America and the Indian subcontinent. The prevalence of these 2 species is approximately equal in South America, Eastern Asia, and Oceanian.<sup>2</sup>

Transfusion-associated malaria is a potentially serious complication that continues to pose risks in blood bank settings. Nearly all cases have been reported from endemic parts of the World. Therefore, Saeed et al<sup>3</sup> suggests that effective malaria screening of blood donations may improve the current exclusion policies of potentially infected carriers on the basis of clinical and travel history. Advani and Banavali<sup>1</sup> reported 99 patients who received cytotoxic therapy for acute leukemia and were retrospectively studied to determine the pattern of infection at the Tata Memorial Hospital, Bombay, India. In all, 224 infective episodes have been reported in these patients. Bacterial infection was the most common type of infection, accounting for 67.9% infective episodes, followed by fungal (15.6%) and viral infections (14.3%). Gram-negative organisms were the most common bacterial organisms isolated, constituting 38 (76%) of 50 positive cultures; infection with *Staphylococcus* was rare (10%). Infectious hepatitis was responsible for fever in 20 patients, malaria in 4 patients and systemic tuberculosis in 2 of the neutropenic patients in that study.<sup>1</sup> Kumar et al<sup>4</sup> also reported 31 patients from India that were microscopically diagnosed with *Plasmodium falciparum* infection complicating hematologic malignancies in children. Salutari et al<sup>5</sup> reported the case of unusually early infection by *P.vivax* after autologous bone marrow transplantation in a 20-year-old female from Bangladesh affected by acute myelogenous leukemia in first complete remission.

Our patient represents a case of febrile neutropenia due to malaria, which is an unusual condition in a non-endemic area. Due to the high incidence of malaria in some geographic areas, it should be kept in mind in the differential diagnosis of febrile neutropenia, and all blood donors, living in high-risk areas, should be suspected and examined for malaria.

Received 8th December 2003. Accepted for publication in final form 9th February 2004.

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The effect of rifampicin on serum cortisol level in patients with active tuberculosis

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**T**uberculosis (TB) is a generalized disease of which no organ or system in the human body is immune. Addison's disease is due to TB infection of the adrenal glands caused by hematogenous spread from a primary focus of infection, which in most cases is the lung. This type of TB infection is known for its debilitating effect in patients causing severe wasting, anorexia, hypotension and pigmentation of areas of skin and mucous membranes by its effect on hormonal production of the adrenal glands.

Rifampicin, which was introduced for the treatment of TB in the 1970's was known to reduce serum levels of cortisol in normal individuals as well as in tuberculous patients who are not suffering from adrenal infection through its action as a potent enzyme inducer.

The aim of this prospective study is to evaluate the serum cortisol levels in patients with pulmonary TB before and 2-3 weeks after the start of anti-TB treatment with a regimen containing rifampicin. Basal serum cortisol levels were estimated on 15 consecutive adult patients with radiologically and bacteriologically proven pulmonary TB before starting treatment and 2-3 weeks after commencement of anti-TB therapy with a regimen containing rifampicin 600 mg first thing in the morning on an empty stomach. All blood specimens were taken at 9 in the morning. **Table 1** shows serum cortisol levels on 15 patients with active pulmonary TB. Basal serum cortisol level before commencement of treatment taken at 9 in the morning were all within or above the normal range of 170-720 nmol/l for 14 out of 15 patients with a mean value of 556 nmol/l. Only patient number 2 had a low basal cortisol level. Two to 3 weeks after commencement of treatment with a regimen

containing rifampicin, the basal serum cortisol levels were lower than the level before commencement of treatment in 12 out of 15 patients, but were nevertheless within the normal range. The mean fall of 71 nmol/l was statistically significant ( $p < 0.05$ ). Three patients including patient 2 showed rise of their basal cortisol levels after treatment. A short Syncthen test performed on patient 2 revealed a normally responsive adrenal gland. In our earlier report of 2 patients with acute adrenal crisis following rifampicin therapy<sup>1</sup> we suggested that by its action as an enzyme inducer, rifampicin was responsible for the fall of serum cortisol levels in patients with compromised adrenal function due to TB infection. This prospective study has shown that abnormal adrenal function is not a common clinical problem (one out of 15). It has also shown that rifampicin therapy can induce a fall in basal serum cortisol levels. Such a fall as seen in our previously reported cases can lead to the development of acute Adisonian crisis in patients with border line adrenal function. Keven et al<sup>2</sup> measured basal adrenal function and adrenal reserve during and after treatment with rifampicin in patients with active tuberculosis. They concluded

Table 1 - Basal serum cortisol before and 2-3 weeks after the start with rifampicin therapy in 15 patients with pulmonary tuberculosis.

| Patients | Basal serum cortisol level before therapy nmol/l | Basal serum cortisol level 2-3 weeks after therapy nmol/l |
|----------|--|---|
| 1        | 732  | 251   |
| 2        | 149  | 265   |
| 3        | 504  | 362   |
| 4        | 492  | 401   |
| 5        | 1031   | 502   |
| 6        | 739  | 323   |
| 7        | 502  | 493   |
| 8        | 657  | 538   |
| 9        | 789  | 546   |
| 10       | 470  | 827   |
| 11       | 712  | 660   |
| 12       | 660  | 350   |
| 13       | 467  | 472   |
| 14       | 724  | 490   |
| 15       | 725  | 587   |

that although impairment of adrenal function is a rare condition in active tuberculosis, rifampicin may have a significant negative effect on steroid metabolism. Okudaira et al<sup>3</sup> described a case of partial Addison's disease in a patient with TB disclosed by rifampicin therapy. They advised that patients with insufficient adrenal response, should be given hydrocortisone while taking rifampicin. Ellis et al<sup>4</sup> studied 41 African Zulus with acute pulmonary TB and found sub-optimal cortisol response to Syncathen and low plasma dehydroepiandrosterone levels. Following anti-TB therapy those who did not receive rifampicin showed improved response to Syncathen test while the response of those on rifampicin was less than expected. Barnes et al<sup>5</sup> however studied 90 Melanesian adult patients with active TB and assessed their adrenal function before and 3-4 weeks after starting anti-tuberculosis therapy. They found normal or raised basal serum cortisol levels; after Syncathen stimulation adrenal response was normal in 92% of the patients and subnormal in 8%. They conclude that abnormal adrenal function is an uncommon problem in active TB and that contrary to recent reports anti-TB chemotherapy regimens that included rifampicin do not have an adverse effect on adrenal function. All these studies including the study of Barnes et al agreed that affection of the adrenal glands can occur in patients with TB resulting in abnormal or sometimes borderline adrenal function. These are the patients in whom rifampicin by its strong action as an enzyme inducer will tip the precarious balance towards acute adrenal failure. In a letter to the *Lancet* on unexpected death due to TB,<sup>6</sup> we expressed our concern that the sudden death of some of our TB patients could be explained on the basis of the effect of rifampicin on serum cortisol metabolism.

In the third world most cases of TB present very late in the course of their disease with asthenia and debilitation and most medical facilities where these patients are treated cannot perform sophisticated investigations such as serum cortisol levels or other adrenal function tests. My message to doctors in such hospitals is to be on the look-out for symptoms and signs of hypoadrenalism in their patients before they succumb to acute adrenal crisis.

**Acknowledgment.** The author would like to thank Mr. Nour A. Elbadawi from the Department of Biochemistry, Faculty of Medicine, Kassala University, Sudan, for preparation of the electronic manuscript.

Received 8th July 2003. Accepted for publication in final form 9th February 2004.

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## Erratum

In manuscript "Intestinal parasites among presumably healthy individuals in Lebanon", Saudi Medical Journal 2004; Vol. 25 (1): 34-37, the *Escherichia coli* (3.8%) in the results section of the abstract should have appeared as *Entamoeba coli* (38%).