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On page 247, the following tables should have appeared as follows:

Table 4. Summary of effects of pharmacological agents on bone mineral density and fracture risk according to randomized, controlled trials.

Agent(s)	BMD	Hip fractures	Vertebral fractures	Other Fractures
Alendronate/risedronate	↑	↓	↓	↓
Calcitonin	↑	N/D	↓	N/D
Calcitriol	↑	N/D	↓	↓
Calcium	↑	N/D	↓	N/D
Hormone replacement therapy	↑	↓	↓	↓
Raloxifene	↑	N/D	↓	N/D

N/D: Not demonstrated (No effect demonstrated, or evidence is not conclusive).

Table 5. Recommendations for treatment of osteoporosis.

BMD with T score above –1, or a FRACTURE Index score with BMD of <6
- Calcium and vitamin D
- Exercise and other lifestyle changes
- Consider follow-up BMD assessment in 5 years, if indicated

BMD with T score –1 to -2.5
- Calcium and vitamin D
- If there is history of fracture(s), or >1 strong risk factor for fractures, or a FRACTURE Index score with BMD 6, consider treatment with a bisphosphonate, SERM, HRT, or calcitonin, as appropriate.
- Consider a follow-up BMD assessment in 2 years, particularly if patient is not receiving pharmacological therapy

BMD with T score below -2.5
- Calcium and vitamin D
- If there is a history of fracture(s), or 1 strong risk factor for fractures, or a FRACTURE Index score with BMD 6, treat with a bisphosphonate, SERM, HRT, or calcitonin, as appropriate
- Consider a follow-up BMD assessment in 1-2 years

Article in full: **http://app.kfshrc.edu.sa/annals/Articles/24_4/03-175.pdf**

and public health resources. The specific reasons for this were explained in length in our article. One example is whether to screen all postmenopausal women at or after age 65 with BMD (level 1 evidence) or to modify this recommendation to account for an earlier development of osteoporosis in our population (according to local studies). Also, we felt it important to account for the clear difference in physical activities and therefore risk of falling between elderly females (above 65) in this region compared to the West. A more reasonable recommendation in our view would be to start screening at an earlier age, and to incorporate risk factors to identify those at higher risk instead of drawing a fixed line that might fit other societies. In contrast, the use of anti-resorptive agents in patients with osteopenia without good evidence that it would decrease fracture rates seem less reasonable in a society with widespread osteopenia but lower fracture rates than the West. A reasonable recommendation in our view again would be to be more conservative in this group, and only to use such expensive treatment when there are fractures or high risk factors. Some international guidelines have recommended treatment for such patients.

In fact, there are significant differences in the recommendations made

by reputable international groups which make it impossible for a practitioner to decide which one to follow. These differences are partially due to different circumstances, resources, views, and even interests. Our task force final recommendations were, therefore, in general agreement with other international evidence-based guidelines. Modifications were only made when felt necessary by reviewing local data.

Finally our attempt was, to our knowledge, the first of its kind in this region that attempted to deal with this ever expanding and often confusing health problem. The guidelines are far from perfect, and obviously are limited by sparse local data and missing information on local risk factors and BMD/fracture correlation. Nevertheless, the guidelines have been very well received by local and even international specialists and practitioners, and are largely adopted by the Saudi Osteoporosis Society, which is in the process of formulating national guidelines.

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Epidemiological, clinical, diagnostic and therapeutic survey of 686 cases of brucellosis

To the Editor : Brucellosis is a zoonosis transmitted to humans from infected animals, mainly after consumption of unpasteurized milk and milk products and less often after direct contact with infected animals via inhalation, especially by children and by slaughterhouse, farm, and laboratory workers.[1,2] Although brucellosis in domestic animals has been controlled in most developed countries it remains an important public health problem in several parts of the world. The disease is endemic in Iran[6-8] as well as in other Middle East and mediterranean countries, and in Latin America.[3-5] In a study in Iran most cases were caused by *Brucella melitensis* usually belonging to biotype I.[8] The aim of this study was to examine the epidemiological features, clinical and hematological characteristics, complications and treatment outcome of brucellosis in Yazd.

We reviewed the records of 686 patients 1 to 70 years of age with the diagnosis of brucellosis over a 6-year period between 1995 and 2001. The Nikoopour clinic is the center for infectious diseases control in Yazd and is also the referral center for patients from other cities, mainly Maybod, Ardakan, Taft, Mehriz, and Sadough. Confirmed cases were defined those with clinical symptoms and signs suggestive of brucellosis in which *Brucella* was recovered from blood. The presumptive diagnosis of brucellosis in patients with negative cultures was based on a standard tube agglutination titer (STA) (1:320. A *Brucella abortus* suspension was used for the STA test.

There was a significant difference in the number of patients during the 6 years of the study; the most were in 1998 with 266 cases (38.8%) and the least in 2001 with 18 cases (2.6%). Males were more commonly affected than females and the male-to-female ratio was 1.32. Only 3.2% of the patients were (5 years of age, and 23.8% were 5 to 14 years). A seasonal variation in the distribution of cases was observed, and the most common cases were observed in summer. Mean (±SD) duration of symptoms prior to diagnosis was 14.1 (±14.6) days (median 11 days, range 7-70 days).

Nearly all patients were febrile, most with moderate fever. Other common symptoms included fatigue, arthralgia, night sweats, gastrointestinal manifestations such as abdominal pain and constipation and diarrhea and weight loss. A substantial number of patients (61%) developed arthritis or arthralgia. The joints more commonly affected included the knee in 49%, hip in 41%, ankle in 18%, wrist in 13%, and small joints of the hand in 15%. Monoarthritis and oligoarthritis was noted. A substantial number of patients (36%) developed sacroiliitis. Arthritis of the cervical spine was rare. The response of joint symptoms to treatment was immediate and by two weeks of treatment nearly all patients had significant improvement. Hepatomegaly was reported in 5% patients. Splenomegaly was recorded in 20% cases and was also mild to moderate. Unilateral or bilateral epididymoorchitis was seen in 11 (2.8%) cases in males.

The antibody titers to *Brucella* determined by standard tube agglutination were as follows: 1/2560, 28 (4.08%); 1280,132 (19.24%); 1/640, 162 (23.62%); 1/320, 204 (29.74%); 1/160, 111 (16.18%); 1/80, 38 (5.54%); 1/40, 11 (1.6%). All of the patients had symptoms and signs suggestive of brucellosis. In patients who had an initial SAT titer of 1/80 the diagnosis was documented with a positive blood culture in 9 or with increased titer to 1/320 or greater on reexamination 1-2 weeks later.

All patients received a combination of two or three antibiotics. Duration of treatment was 8-12 weeks. None of the patients was readmitted to our clinic with a relapse. Only four patients had been previously treated in other places and presented for the first time to our clinic with a relapse. Two had received doxycycline and streptomycin for 2 weeks and two received doxycycline and rifampicin for 2 weeks. All four patients relapsed twice 1 to 2 months after discontinuation of therapy. They were then treated with doxycycline and streptomycin for 4 weeks and then with doxycyline and rifampin for 8 weeks and had no relapse during 6 months of follow-up.

Remarkable and unusual complications were noted in two patients who developed chronic meningitis

and endocarditis. The first patient developed a prolonged history of fatigue and weight loss and night sweats and low-grade fever. Blood cultures were negative and STA titer in the first 2 months was negative or 1/40. However, in the third month STA was detected at 1/640 and the CSF STA test was 1/80. The second patient presented with fever and sweats and weight loss, but the serum titer of the STA test was 1/40 and blood cultures were negative. However, one month after initiation of signs and symptoms the STA titer was detected at 1/640 and ultimately a heart murmur was detected.

Brucellosis is a systemic disease with protean manifestations. Its features may mimic those of other febrile illnesses. Brucellosis remains an important public health problem in our area and can cause serious complications, resulting in significant morbidity. The clinical characteristics of brucellosis in our series are similar to those reported by previous studies.[1,7] Musculoskeletal manifestations were recorded in the majority of patients and included arthralgia and arthritis, which most commonly affected the large joints of the lower extremities. Sacroiliitis was a frequent manifestation of brucellosis in our patients, but arthritis of the small joints of the hand was infrequent. The response of joint symptoms to treatment was immediate in our patients and none suffered long-term complications.

The most common hematological manifestations of brucellosis in our group of patients were a normal CBC followed by anemia and lymphocytosis. These hematological manifestations of brucellosis have been reported in previous studies.[1,2] Leukopenia was less frequently encountered in our series.

A remarkable finding of the study was the insignificant STA titer (1/80) in a considerable number of patients (49, 7.14%), in whom the diagnosis was confirmed with a positive blood culture (9 cases) or with an increase in titer to 1/320 or greater on reexamination 1 to 2 weeks later. A falsely low or equivocal STA titer occasionally occurs in patients with acute brucellosis and the diagnosis can be made with the detection of IgM antibodies with ELISA[1-9] or culture or repeat STA later. [1-2]

Neurological complications of brucellosis are uncommon[1,10-12] and occur in <5%. In our study only one patient developed chronic meningitis. Blood cultures were negative and the STA titer in the first 2 months was (1/40). However, in the third month STA were detected at 1/640 and the CSF STA test was 1/80.

Our patients were treated with different therapeutic regimens and duration of treatment was variable since this was a retrospective study spanning 6 years. However, none of the patients who received a combination of rifampicin plus either doxycycline or trimethoprim- sulfamethoxazole ± streptomycin (for the first month) for 8 weeks or longer had a relapse. Therefore, it appears that the combination of at least two of the above antibiotics for a period of 8 weeks is an effective treatment for brucellosis. The patients who presented with a relapse had previously received a combination of two antibiotics for 2 weeks. The relapse occurred in these patients within 1 to 2 months from completion of initial treatment. High relapse rates have been reported with short-term (3 week) two-drug regimens even when an aminoglycoside was initially included.[7-14]

In conclusion, brucellosis has a wide range of clinical manifestations. It may affect any organ system and imitate a variety of clinical entities. Physicians practicing in endemic areas must be familiar with this disease so that early recognition results in lower morbidity. The diagnosis may present difficulties since blood cultures or the agglutination test may not always be positive. Treatment with at least two antibiotics for not less than eight weeks appears to be effective. An organized effort must be undertaken in endemic areas for brucellosis control through vaccination of animals and finally eradication through testing and slaughter of infected animals.[13-14]

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A neonatal case of citrullinemia with urolithiasis

To the Editor: Citrullinemia is a rare autosomal recessive inborn error of urea cycle metabolism caused by a deficiency of argininosuccinate synthetase. At least half of genetically affected newborns present in the first several days of life. Major clinical symptoms and signs of hyperammonemia in the neonatal period are difficulty in feeding, vomiting, tachypnea, lethargy, convulsion and coma. The neonatal forms are serious and many times are associated with a high level of mortality.[1] We describe a neonatal case of citrullinemia associated with urolithiasis.

A 2900-g baby showed symptoms of hypotonia, tachypnea and difficulty in feeding on the third day of his routine care in the maternity ward of our clinic after an uneventful vaginal delivery. With these symptoms, the patient was screened for sepsis. All the culture results were negative after 48 hours. On the 4th day, he developed left-sided clonic convulsions. The seizures did not respond to intravenous dormicum (midazolam) and phenytoin. Arterial blood gas analysis was normal. Blood was taken for serum ammonia level and a metabolic screen. Subsequent development of apnea and dilated poorly responsive pupils led to intubation and mechanical ventilation. Laboratory results included severely elevated ammonia (619 mol/L). The citrulline level was extremely elevated by the tandem mass spectrophotometer and the urinary citrulline level was also found to be extremely elevated. No peak belonging to argininosuccinic acid was seen. Quantitative analysis of plasma amino acids revealed citrulline to be 1142 µmol/L (10-45) which was extremely elevated. The patient was treated by hemodialysis and enteral sodium benzoate because of his high ammonia level.

Because citrullinemia can be associated with multiple congenital anomalies and organ disease, an ultrasonographic (US) evaluation of the cranium and abdomen was performed.

Cranial US was normal. The abdominal US revealed calculi at the distal end of the left ureter and right renal pelvis.There was a history of parental consanguinity. The patient was lost on the tenth day of admission to the neonatal intensive care unit due to encephalopathy.

Argininosuccinic acid synthetase deficiency (ASD) is a rare disorder of urea cycle metabolism, with pronounced citrullinemia.[1] The prognosis depends on early diagnosis, which is based on clinical suspicion and analytical determination of ammonia in every newborn with unexplained vomiting, lethargy or other symptoms of encephalopathy.[2]

Many anomalies and organ disease have been reported in surviving citrullinemia cases, including transposition of the great arteries, subarachnoid hemorrhage, intracranial anomalies, intrahepatic cholestasis, and cutaneous manifestations are some of the anomalies reported in the literature.[1-4] In conclusion we want to emphasize the association of the disease with urolithiasis so that renal calculi are kept in mind in cases who survive.

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On page 306, the following name and address of the author should have appeared with the article "Thoracic ectopia cordis (naked heart)":

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