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To the Editor:

The "cross-sectional index" developed by Dr. Gryfe and his colleagues may well provide a more accurate estimate of general skeletal mineralization in the individual patient than the simple measurement of cortical thickness. However, when grouped data are being compared the two methods are likely to yield essentially the same results unless there is a marked difference in the average stature of the groups being compared.

Concerning duration of residence, this is but one of several variables that would need to be controlled before any firm conclusions could be drawn about a causal relationship between local water supply and body composition — others being the (life-long?) type and quantity of diet, the amount of water actually consumed, etc. An investigation that took all these factors into account would be very costly, both in time and resources, and the entirely negative results that were obtained in the recent study lead me to believe that such an elaborate and expensive investigation would not be justified.

T. W. ANDERSON, M.D., PH.D.
School of Hygiene,
University of Toronto,
Toronto 5, Ont.

Nalidixic acid arthralgia

To the Editor:

We wish to draw attention to what we believe to be a rare and possibly unreported complication of nalidixic acid (NA) therapy, namely, a crippling, flitting arthralgia which completely reversed after withdrawing the agent. On two occasions the same patient also developed the bizarre visual and neurological phenomena which are not infrequent when the recommended "full" dosage of 1 g. every six hours is prescribed.

Case report:

The patient, a 22-year-old married white woman, had suffered recurrent urinary tract infections since becoming sexually active at age 20 years. The first two episodes presented as cystitis, while on four subsequent occasions (including one when 28 weeks pregnant) the attacks of lower urinary tract symptoms were associated with fever (>37.8°C), rigors and bilateral loin pain with tenderness (acute pyelonephritis). The third episode of acute pyelonephritis was treated with NA. After the second 1 g. dose she became delirious and noted striking subjective visual disturbances including difficulty in focusing, overbright lights, an alteration in colour perception and visual hallucinations. All the symptoms settled rapidly when the drug was discontinued. Extensive urinary tract investigations and tests of renal function revealed no abnormalities.

In May 1972 the patient again presented with acute pyelonephritis and NA in a dose of 0.5 g. every six hours was prescribed. After four doses she developed severe arthralgia with joint swelling, redness and limitation of movement which started in the small joints of the right foot and ankle, then spread to the left foot and later to the knees, hands, wrists, elbows and right shoulder. Her doctor thereupon doubled the dosage following which the patient developed the visual and neurological disturbances which she had suffered after previous 1 g. doses, as well as nightmares and episodes of inappropriate crying. She also noted general weakness, lethargy and loss of appetite. After three days she was admitted to hospital and the drug was discontinued. On admission she was febrile (37.8°C), appeared pale, had slightly injected fauces and three small tender glands in the right axilla. She was unable to move because of extremely painful joints; the interphalangeal (especially proximal) joints of both hands and to a lesser extent both feet showed fusiform swelling and were warm, red and tender. The arthralgia reached a peak 36 hours after the NA had been discontinued and over the next 17 days the patient recovered completely without disability. Extensive hematological, biochemical, immunological and radiological investigations were normal apart from a mild iron deficiency anemia of 11.1 g./100 ml., an erythrocyte sedimentation rate of 97 mm./hr., total serum protein of 5.9 g./100 ml. with 2.7 g./100 ml. albumin and a serum alkaline phosphatase of 132 mU./ml. (normal 30-85). A specimen of urine obtained by suprapubic bladder aspiration contained no red cells, 15 white cells/c. mm., a trace of protein and was sterile. Four weeks after discharge from hospital she was well with no residual signs. A full laboratory work-up revealed no abnormalities apart from an erythrocyte sedimentation rate of 39 mm./hr.

We consider the incapacitating arthralgia from which this young woman suffered to be a severe allergic manifestation to NA and one which we have not previously seen. The manufacturers (Dr. Joyce Abel, Medical Director, Winthrop Laboratories, Aurora, Ontario: personal communication) have on record about a dozen reports of side-effects relative to the joints — arthralgia or joint swelling, occasionally accompanied by a rash and/or fever. In one case[1] a child developed soreness of one wrist after two widely-spaced courses of NA treatment. No local swelling was observed and prompt symptomatic improvement followed withdrawal of the drug on each occasion. Several of the cases were believed not to be due to the nalidixic acid therapy and few, if any, have been as severe as the one which we report.

Many of the commoner side-effects attributed to NA (especially those relating to the gastrointestinal tract) are in our opinion due to the excessive daily dosage of the drug as recommended by the manufacturers. These frequent side-effects have resulted in the drug becoming unpopular in some centres but in our experience NA is equally effective in a dose of 0.5 g. every six to eight hours for seven days[2] and eradicates over 90% of UTIs due to sensitive organisms in women with a radiologically normal urinary tract and normal renal function. This reduced dosage virtually eliminates the troublesome side-effects of the drug. Our clinical observations compare favourably with the results of the recent multicentre study undertaken in the United Kingdom where the sensitivities of 23,491 urinary tract pathogens were assessed.[3] In this study NA performed very creditably and comparably with nitrofurantoin and cotrimoxazole (sulfamethoxazole-trimethoprim). NA is however rather ineffective in UTIs due to gram-positive organisms.[4] Of 121 strains of coagulase-negative staphylococci obtained by suprapubic aspiration from women with urinary tract infections, only 41% were sensitive to NA on *in vitro* testing (Bailey and Roberts: unpublished data).

NA is also a useful agent in renal failure, principally because the clearance of the therapeutically active naphthyridines is not related to renal function and even if renal impairment is severe, antibacterial levels are usually reached in the urine.[5] The clearance of the inactive conjugates is however decreased in renal failure, resulting in an elevation in the plasma levels; prolonged courses of full dosage should therefore be avoided.

Finally it has been widely dissemi-

nated in the literature that rapid high-grade bacterial resistance frequently develops to NA. In our experience this is rare and in fact we are unaware of a single episode where NA resistance has been transferred by R factors. Of importance is the fact that the NA-sensitivity pattern for the common urinary tract pathogens has not changed since the agent was introduced 10 years ago.[6] Very few of the papers claiming this problem of resistance have produced adequate evidence that the resistant organisms were serologically identical to the previously sensitive strains.[6]

In summary we regard NA as a very effective and relatively safe drug in a dose less than that recommended by the manufacturers, but even at this reduced dosage severe allergic phenomena may develop.

Ross R. Bailey, M.D., CH.B., M.R.A.C.P., M.R.C.P.[UK]
Renato Natale, B.SC.
Adam L. Linton, M.B., F.R.C.P.[EDIN and GLAS]

Renal Unit, Victoria Hospital, and
Department of Medicine,
University of Western Ontario,
London, Ont.

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Faith in healing

To the Editor:

I am editing a book on the role of faith or religion in healing from a physician's standpoint. I would appreciate it if anyone interested in writing for this book would contact me.

Claude A. Frazier, M.D.
4-C Doctors Park,
Asheville, N.C. 28801

Enteral hyperalimentation with elemental diet

To the Editor:

I would like to add certain information to that provided in the editorial "Enteral hyperalimentation with elemental diet" (*Can Med Assoc J* 107: 184, 1972).

In 1967 two studies on dogs reported from the surgical laboratories of the Montreal General Hospital showed that the use of an elemental semihydrolyzed diet before and after injury could minimize the extent of the intestinal lesions and improve the chances of survival following shock or intestinal ischemia.[1, 2] The elemental diet used was made up essentially of fibrin hydrolysate, sucrose and Lipomul. On the basis of the findings in these studies the Mead Johnson Company of Canada Ltd. was encouraged in 1968 to explore the potential clinical uses of elemental diets in a wide range of catabolic states of intestinal or extra-intestinal origin. Making use of experience gained with such other semi-elemental diets as Nutramigen and Portagen they began a long search for an ideal alimentary product which would provide the maximum amount of hydrolyzed constituents in a palatable mixture which would meet the nutritional requirements of humans to be fed exclusively on such a diet for prolonged periods of time. The company finally developed the product 3200-AS now known as Flexical which was released for testing towards the end of 1969 to the Montreal General Hospital and the Centre Hospitalier Universitaire in Sherbrooke. It was canned in powder form.[3-5] Actually the first batch differed from Flexical only in that it contained 17% casein hydrolysate; to improve the palatability the casein hydrolysate was later reduced to 10%. This prototype was shown to be as effective as our previous diet[1] in protecting animals in shock.[6] In all subsequent studies the elemental diet used was Flexical with changes limited to miscellaneous ingredients to improve flavour and texture.[3-5, 7] An elemental diet could not be adequately tested in man until a suitable product was developed; this was in early 1970.

In reference to the statement "The role of elemental diets . . . in the protection of the gut from radiation and chemotherapy-induced injury remains to be explored. Well controlled studies using liquid diets of the same composition but in elemental and non-elemental form will have to be carried out . . ." it should be noted that experimental work and a preliminary clinical study reported about a year ago have shown a certain prophylactic effect of the elemental diet upon the intestinal lesions associated with radiation[3, 4] and chemotherapy.[3, 8] In these studies[4, 8] the protection afforded by the elemental diet was found to depend specifically on the protein hydrolysate substituted for whole casein. In a study on human volunteers we compared two liquid elemental diets whose essential difference was substitution of casein hydrolysate for whole casein.[7] For such studies it is important to be aware that Flexical can be administered for at least 12 days without pancreatic damage or hemolytic anemia as was the case in animals receiving pure amino acids instead of protein hydrolysates for longer periods of time. At the Centre Hospitalier Universitaire we also used Flexical in patients with severe burns, intestinal fistulas, regional enteritis, short bowel and pancreatitis. Our results are in agreement with those of Bury and his colleagues[9, 10] and Voitk *et al*[5] indicating that elemental diets may be an effective adjuvant in the nutritional management of critically ill patients. The diet was usually given by mouth at the recommended osmolarity of about 700 mOsm/l. (1 cal./ml.). In patients whose gastrointestinal tracts have been reduced in length or have had bypass operations, an osmotic diarrhea may ensue. This complication usually subsides after proper dilution of the diet and intestinal adaptation. In patients receiving intravenous hyperalimentation and no water by mouth, serum osmolarity must be controlled daily. Since the solution is hyperosmotic, the rate of administration should not exceed the rate of metabolism and excretion in order to prevent an increase in the osmolarity of the extracellular fluids.

Gustave Bounous, M.D.
Centre Hospitalier Universitaire,
Sherbrooke, Que.

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