parathyroid hormone concentration 0.6 ng/ml (normal <1.0); and 25-hydroxycholecalciferol concentration 46 nmol/l (18.5 ng/ml) (normal 10-75 nmol/l; 4-30 ng/ml). Blood gases, amino-acids, urea and electrolyte concentrations, and results of ophthalmic slit-lamp examination were normal. Urine pH was 5.0; calcium concentration was under 1 mmol/l (4 mg/100 ml) and phosphate concentration 13.4 mmol/l (41 mg/100 ml).

The patient was treated with vitamin D and oral phosphate, which were serially adjusted to heal the rickets and prevent hypercalcaemia and hypophosphataemia (figure). When she was aged 5 years 1 α -hydroxy vitamin D₃

Serial calcium and phosphate concentrations and alkaline phosphatase activity related to treatment from 23 months of age onwards.

Conversion: SI to traditional units—Calcium: 1 mmol/l $\approx$ 4.0 mg/100 ml. Phosphate 1 mmol/l $\approx$ 3.0 mg/100 ml.

was substituted for vitamin D and simultaneously phosphate supplements were stopped. Serum phosphate concentrations promptly fell, and alkaline phosphatase activity rose. After 11 months radiography of the wrists showed no abnormality, but the knees showed florid rickets. Phosphate supplements were restarted, reversing the hypophosphataemia and hyperphosphatasia, and the rickets healed. The doses of 1 α -hydroxy vitamin D₃ and phosphate were serially adjusted to maintain normal serum concentrations of calcium and phosphate. She was overactive with difficult behaviour during the hypophosphataemic period. Her height gradually increased from the first to the tenth centiles over the five years of treatment. The initial bowing of the femora cleared and she lived an otherwise normal schoolgirl life.

The child continued with the same dose of 1 α -hydroxy vitamin D₃ as when rickets was present, yet she was normal with the help of phosphate supplements.

Comment

Vitamin D increases the absorption of dietary calcium and phosphate but does not prevent the excessive renal loss of phosphate that is characteristic of hypophosphataemic vitamin-D resistant rickets.¹ Recent reports suggest that the condition is well controlled using 1 α -hydroxy vitamin D₃ in high pharmacological doses of 0.5-2.0 μ g/kg body weight daily.^{2,3} Our patient developed hypercalcaemia with only 0.1-0.15 μ g/kg body weight daily and the danger of hypercalcaemia increases with higher doses. The highest recorded serum phosphate concentration in children treated with 1 α -hydroxy vitamin D₃ alone was 0.97 mmol/l (3.0 mg/100 ml), the normal childhood range being 1.3-1.9 mmol/l (4.0-6.0 mg/100 ml).² In similarly treated adults the mean serum phosphate concentration was only 0.76 mmol/l (2.3 mg/100 ml), the normal adult range being 0.8-1.3 mmol/l (2.4-4.0 mg/100 ml).³ Our patient developed normal concentrations only when phosphate supplements were given. Her abnormal overactive behaviour during the hypophosphataemic phase accords with the known whole-body effects of hypophosphataemia.⁴

Population surveys for rickets depend radiologically on pictures of wrists but our experience with this child shows the importance of also including the knees.⁵ We suggest that the logical method of treating this condition is with low doses of 1 α -hydroxy vitamin D₃ to-

gether with phosphate supplements. The likelihood exists that phosphate will prove equally necessary in the treatment of other forms of renal hypophosphataemic rickets.

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Departments of Child Health and Medical Biochemistry, University Hospital of Wales, Cardiff CF4 4XN

H V PRICE, FRCP, DCH, lecturer in child health

J S WOODHEAD, PHD, senior lecturer in medical biochemistry

Role of tartrazine in chronic urticaria

Reactions to azo dyes, particularly the yellow dye tartrazine, are often reported. The proportion of patients with chronic urticaria who develop an exacerbation after taking tartrazine has ranged from 5 to 36%.^{1,2} Salicylates, usually in the form of aspirin, will cause similar exacerbations, affecting 20-45% of patients with chronic urticaria.³ Many patients who have a reaction to salicylate in an active phase of chronic urticaria can take salicylates again when the urticaria is clear.

When patients with chronic urticaria are challenged with a battery of substances, including salicylates and tartrazine, those who react to one are frequently affected by the other.⁴ We tested 317 patients: 40 (13%) reacted to tartrazine and 28 of these also reacted to salicylates. The mechanisms of tartrazine and salicylate reactions in chronic urticaria are probably similar and non-immunological. This view would be strengthened if it was shown that patients who had previously developed exacerbations of urticaria owing to tartrazine no longer reacted once their urticaria was clear.

Patients, methods, and results

From 40 patients with chronic urticaria who had previously reacted to 10 mg tartrazine we selected 20 who lived near Bristol. Thirteen agreed to come to hospital for further tests but one defaulted, so that the tests were carried out in 12 patients (seven women, five men; average age 44 years, range 17-71). Each patient was given three identical capsules—lactose, tartrazine 10 mg, and lactose—which were taken on alternate mornings. One to four weeks later a test dose of 1 mg tartrazine was given interspersed with two other colours as part of a different investigation.

The development of widespread weals between two and eight hours after the capsule was taken was recorded as a positive reaction. Five patients who had been clear of urticaria for one-and-a-half to seven years had no reaction to 10 mg and 1 mg tartrazine; two who had been clear for two to three years except for minor episodic attacks had no reaction to 10 mg and 1 mg tartrazine; and three who had been clear for three to eight weeks showed a reaction to 10 mg tartrazine but none to 1 mg tartrazine. Two patients still with active urticaria (present for three and seven years) showed reactions to both 10 mg and 1 mg tartrazine.

Comment

In the 12 patients tested reactions to tartrazine occurred when the urticaria was in an active phase or shortly afterwards, and did not occur when the urticaria had been clear for a long period. The effect is quantitative since the two patients reacting to 1 mg tartrazine were the only ones with active urticaria. In another series of 56 patients with chronic urticaria⁵ immediate and 48-hour patch tests were carried out to 2% tartrazine. These were all negative, including in four patients who had reacted to oral challenge tests of 10 mg tartrazine.

The reactions to tartrazine seem to have many features in common with the more frequent reactions to salicylates. Both occur when the urticaria is active, and when patients have been clear for some time they are able to take salicylates and tartrazine without producing weals. Thus these reactions are probably due not to an allergic mechanism but to some pharmacological action. Presumably tartrazine and salicylates have some non-specific effect on the production of metabolites leading to development of the urticarial weals.

The prevalence of reactions to tartrazine in patients with chronic urticaria is about 10%, and once the phase of urticaria has been settled the patients can again take tartrazine without trouble. It would seem that the overall dangers from tartrazine in foods and drugs have been exaggerated, certainly in patients with urticaria.

We thank Beecham Research Laboratories for advice and for providing capsules of tartrazine.

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Department of Dermatology, Bristol Royal Infirmary BS2 8HW

ROBERT P WARIN, MD, FRCP, dermatologist

RUTH J SMITH, MB, CHB, clinical assistant in dermatology

Resting pulse rate in marathon runners

In 1935 McKinlay and Walker¹ reported a study of resting heart rate undertaken in Glasgow, which was used by Bradford Hill as an example in all editions of *Principles of Medical Statistics*. It is surprising, therefore, that few subsequent epidemiological studies have included resting heart rate as a variable to predict health or disease.

It is well known that long distance runners have a slow resting heart rate, but we know of no studies reporting more than 50 cases. We measured the resting heart rate of 103 runners in the Cardiff marathon in 1981.

Subjects, methods, and results

Over 3000 people ran in the Cardiff marathon on 20 September 1981, and 95% completed the run in 146 to 465 minutes. The *Western Mail* published the names of 2419 of those who took less than 390 minutes to complete the course. We selected three groups: (1) the first 59 (<182 minutes); (2) the 58 placings 943 to 1000 (240-300 minutes); and (3) the last 57 placings (360-390 minutes).

We sent a postal inquiry to 155 of these people with reliable addresses requesting age, sex, height, weight, smoking habits, and resting pulse rate. A total of 118 (76%) responded, of whom 10 were women, five children, and 103 men. We report the results for men only.

There were no consistent differences in age or height between the groups. At a standardised height of 173 cm subjects in group 1 were 4.5 kg lighter than subjects in group 2, who were 6.0 kg lighter than subjects in group 3. This is in agreement with other reports.² In groups 1 and 2 5% were smokers, compared with 26% in group 3. The mean ($\pm$ SD) resting pulse rates (beats/minute) were 51.0 ± 7.6 in group 1; 62.6 ± 8.8 in group 2; and 67.6 ± 8.7 in group 3. The differences between group 1 and the two other groups were significant ($p < 0.001$); the difference between groups 2 and 3 was in the same direction and approached significance ($p \approx 0.05$). Subjects in group 1 spent 8.7 hours a week in training, in group 2 6.5 hours, and in group 3 5.4 hours.

Comment

Self-reporting of resting heart rate may give rise to inaccuracies. To minimise non-response we did not stipulate how or when it should

be recorded, but we understand that trained athletes usually take their resting pulse rate seated first thing in the morning or, if during the day, after 15 minutes' rest. Recording the resting pulse rate is an integral part of training for runners. Our results are consistent with other studies reporting low resting pulse rate associated with physical fitness. Bond³ found that five runners of Olympic standard had even lower rates.

The figure compares the three groups with the Olympic runners³ and with the Glasgow sample of healthy men.¹ Although the Glasgow sample was not a valid comparison group, some broad inferences may be drawn. Resting pulse rate declines in athletes subject to training, and this is advantageous to completing a marathon in a low time—the lower the resting pulse rate the shorter the time.

Resting pulse rates in groups of marathon runners and a sample of healthy men in Glasgow.

We consider that resting pulse rate may have a wider relevance to health: 25 deaths occur annually on UK squash courts,⁴ and 67 people died in sauna baths in Finland in one year.⁵ Intense activity, emotion, and mental and thermal stresses may raise heart rates to 200 beats/minute. If 180 beats/minute is a safe submaximal limit then a rate of 90 can only double, whereas a rate of 60 may increase three-fold. We suggest that sudden deaths in sport, in saunas, or after stress are more likely in people with higher resting pulse rates.

Clearly, resting pulse rate may be reduced by increasing physical fitness, but it may also be reduced by avoiding smoking. Its importance as an indicator of health, of risk of disease, and of mortality has been neglected in recent epidemiological studies. It deserves more respect and attention.

We thank Mr Tony Barclett, of the *Western Mail*, for the addresses of the runners, and we thank all the respondents.

Full data and a comprehensive bibliography are available on request.

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Department of Medical Statistics, Welsh National School of Medicine, Cardiff CF4 4XN

T KHOSLA, PHD, senior lecturer

H CAMPBELL, FRCP, FFCM, professor of medical statistics