can be prevented from recurring by the administration of adequate amounts of vitamin C."

Clinically, the subperiosteal haematoma, the tenderness and "frog position" of his leg, plus marked radiological changes in rapidly growing bones were characteristic of infantile scurvy. Skin and subcutaneous haemorrhages, and hyperkeratotic hair follicles, seen in older patients, were absent. Anorexia, swollen gums, anaemia, and low-grade fever (probably due to blood-absorption) may be features of scurvy at any age.

Summary

Reference is made to 16 examples of scurvy in infants and children reported from England and Wales in the past 10 years. All but one failed to take a mixed diet containing fruit and vegetables due to (*a*) lateness in weaning (eight infants aged 7 to 12 months), (*b*) mental defectiveness (six children aged 23 months to 4½ years), or (*c*) food faddism (one girl of 10 years), and all were combined with failure to offer orange juice, or a substitute if refused or vomited. Malnutrition due to gastro-enteritis accounted for one at 4 months.

Of 17 adult cases reported over the same period, most were either old men living alone or people on restricted diets chiefly for peptic ulcers.

Scurvy occurring in a 15-months-old boy in an institution is described. The accepted minimum daily vitamin C requirement of 10 mg. had not been met by a mixed diet, including vegetables and a teaspoonful of rose-hip syrup containing about 7 mg. of ascorbic acid.

Reasons for the low dietary content are suggested, and the liability of this to occur in institutions is emphasized.

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"The increasing clarity of the atmosphere has been noted on many occasions during the year; the effects of the steady improvement in the condition of the atmosphere on health will take longer to become evident. Custom and a mistaken conception of comfort are difficult hurdles to overcome, but the response of the public to the measure for clearing the atmosphere has been very encouraging. Privy middens were once usual but are now unacceptable—in twenty years' time people will recount with amused censure and an air of superiority. 'Fancy! they had open coal fires.'" (*Annual Report on the Health of the City of Sheffield*, 1958.)

OBESITY IN CHILDHOOD

A CLINICAL TRIAL OF PHENMETRAZINE

BY

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Phenmetrazine ("preludin") is a synthetic derivative of ephedrine. It is not pharmacologically related to amphetamine. It has been much used in the treatment of obesity owing to its effect on the appetite. According to the manufacturers the primary action is on "the satiety centre in the hypothalamus. Satisfaction of appetite occurs sooner than normal. On the other hand, the urge to eat remains unaffected." The value of phenmetrazine in the control of obesity in adults has been demonstrated by several controlled investigations (Fazekas, Ehrmantraut, and Kleh, 1958; Leith and Beck, 1958; Patterson, 1959). There are also references in the literature to the value of phenmetrazine in the control of obesity in children (Bleckmann and Salus, 1955), but no clinical trial of the use of the drug in children has so far been published. For this reason the present study was undertaken.

Present Investigations

The obese children included in this investigation were treated as out-patients. They all weighed over the ninetieth percentile above the average weight for their age, and all were gaining weight at the beginning of the trial. During the investigation they were on their normal diet.

The children received no treatment during a preliminary period of 14 days. They were weighed at the beginning and at the end of this period. They were then sent to the pharmacist, who selected at random a paper from an envelope. This stated whether the child was initially to be given phenmetrazine or dummy tablets.* Sufficient tablets for 28 days' use were dispensed. The dose of phenmetrazine was 25 mg. in the morning and midday for children aged 8 years and over, and 12.5 at the same times for children under 8. At the end of the 28 days the child was weighed and a further supply of tablets was prescribed. The second set of tablets was the opposite—active or dummy—to that which the child had received previously, so that each child acted as his own control. At the end of the second period of 28 days the child was again weighed and then took no further part in the investigation. The children and their parents did not know that the tablets were different, and only the pharmacist knew which tablets the child received until after the investigation was completed and the results had been tabulated.

Eleven children did not complete the full course and are not included in the series. This was because of two main reasons. (1) Some children failed to return for weighing at exactly the right time because of holidays or for other domestic reasons. Many of these children attended a week later, but as they had been without tablets for a week they could not be included in the trial. (2) Some children had an illness, such as measles or tonsillitis, which probably affected their appetite.

*The phenmetrazine and dummy tablets were kindly supplied by Boehringer Products division of Pfizer Ltd.

Results

The results of the experiment are shown in the Table. Twenty-one children completed the trial. During the first two weeks the children gained between ½ and 5 lb. (227 and 2,270 g.) in weight, with an average of about 2 lb. (907 g.). While receiving phenmetrazine 18 children

Result of Double-blind Controlled Trial of Phenmetrazine

Case No.	Weight Gain During Preliminary Two Weeks (in lb.)	Weight Gained or Lost While Receiving Phenmetrazine (in lb.)	Weight Gained or Lost While Receiving inert Tablets (in lb.)
1	+1	−½	+1½
2	+1	−1	+2
3	+3	Nil	+1
4	+2	−7	−1
5	+3½	−4	+1
6	+3	−2½	Nil
7	+1	−8	+1½
8	+½	−5	+3
9	+1½	−2½	+3½
10	+½	−7½	+1½
11	+3	−4½	−1½
12	+1	−½	+4
13	+1	−3	+2
14	+½	−4	+1½
15	+½	−6	+1
16	+5	−3	+2
17	+3	Nil	+3
18	+1	−6	+1
19	+2½	−1½	Nil
20	+5	−2	+3
21	+1	+4	+5

1 lb. = 454 g.

lost between ½ and 8 lb. (227 and 3,630 g.) with an average of 4 lb. (1,815 g.), two children remained stationary, and one child gained 4 lb. (1,815 g.). While receiving the dummy tablets 17 children gained from 1 to 5 lb. (454 to 2,270 g.) with an average of 2 lb. (907 g.), two remained stationary, and two lost 1 and 1½ lb. (450 and 680 g.) respectively. On studying the figures it will be seen that in every case phenmetrazine was more effective than the dummy tablet. Even the children who did not lose weight while receiving the drug gained more while they were not receiving it; while all the children who did not gain weight while on the placebo lost considerably while taking phenmetrazine.

Only four children failed to gain weight on the dummy tablets. These had gained at least 2 lb. (907 g.) during the probationary two weeks. Three of the four children happened to have the active drug first and the dummy second. These children give some indication of the way in which illicit dieting or minor ailments may have affected the outcome of the experiment.

Discussion

Phenmetrazine, in the dosage given, was a highly effective weapon againt obesity. The result of the experiment is the more remarkable when it is remembered that the children's diet was not restricted and they had been shown to be gaining weight prior to the time they received the drug. None of the children complained of any ill effects, though one child became very ill-tempered while receiving phenmetrazine, and her parents stopped giving her the drug.

Phenmetrazine is not an innocuous drug. Subacute delirium (Silverman, 1959), toxic psychosis (Bethell, 1957), and addiction (Kahan and Mullins, 1958; Evans, 1959) have all been described in adults with psychopathic personalities.

In order to discover the effect of phenmetrazine, no dieting was allowed in the experiment reported above. This does not, of course, mean that diet plays no part in the treatment of childhood obesity. On the contrary, appropriate dietetic measures should be the mainstay of treatment, and only if that fails should phenmetrazine be introduced as a useful adjuvant. No treatment apart from starvation in hospital will succeed unless the child is willing to co-operate. Indeed, as Wallgren (1959) has indicated, it may well be better in some cases for the child to remain fat than to provoke an unnecessary psychological tussle.

Summary

A double-blind controlled trial of phenmetrazine on 21 children receiving an unrestricted diet gave the following results: while receiving phenmetrazine 18 children lost weight, 2 remained stationary, and 1 gained weight. While receiving inert tablets: 17 children gained weight, 2 remained stationary, and 2 lost weight.

The potential dangers of phenmetrazine and the indications for its use are indicated.

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USE OF ^{82}Br IN DIFFERENTIAL DIAGNOSIS OF LYMPHOCYTIC MENINGITIS

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The Bromide Partition Ratio

In 1929 Walter described a method for estimating bromide levels in blood and cerebrospinal fluid (C.S.F.) and showed that in the normal subject there was a blood/C.S.F. barrier. The partition of bromide between blood and C.S.F. could be expressed as a bromide ratio,

$$\frac{\text{bromide per unit volume serum}}{\text{bromide per unit volume C.S.F.,}}$$

which fell within the range 2.9 to 3.5 (mean 3.1). Walter also showed that in tuberculous meningitis and in