An elevated level of serum vitamin B₁₂ in chronic myeloid leukaemia, first reported by Beard *et al.* (1954), has been conclusively confirmed by a number of investigators. The exact cause of this elevated level is not clear. Lack of any differential pattern in the two groups—vegetarian or non-vegetarian—as revealed in the present study, indicates that in this disease the factor responsible for hypervitaminosis far outweighs the hypovitaminic effect of a vegetarian diet.

Summary

The serum vitamin B₁₂ level was studied in 232 subjects (196 non-vegetarians and 46 vegetarians). The subjects belonged to the following five categories: normal, tropical eosinophilia, nutritional macrocytic anaemia, aplastic anaemia, and chronic myeloid leukaemia.

Serum vitamin B₁₂ in the vegetarian group was, in general, lower than that in the non-vegetarian group. Chronic myeloid leukaemia was an exception, all the patients in this category showing a raised level as previously reported.

Low serum vitamin B₁₂ was not, however, associated with any anaemia or neurological complications. The implications of these findings are discussed.

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The Italian Olympic Medical Committee is conducting a statistical study of competitors who took part in the Olympic Games in order to discover the correlations between medical characteristics and performance. To obtain this comprehensive medical data—in all, 78 medical characteristics for each athlete—for at least 2,000 of the 7,000 competitors in this year's games, the medical sections of various national Olympic Committees (including the German, Italian, and Russian) have agreed to supply the results of medical examinations of their athletes carried out in their own countries. Once this information has been collected it will be recorded on punched-cards which will then be processed by the IBM 305 RAMAC computer.

TREATMENT OF RESPIRATORY INFECTION IN SCHOOLBOYS WITH PHENETHICILLIN

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The administration of penicillin to children has hitherto presented several practical problems. Crystalline penicillin by injection gives satisfactory blood levels, but is painful and very unpopular with young patients. Oral penicillins G and V are far more acceptable, but the blood levels obtained are much lower than those achieved by parenteral administration, and are indeed often insufficient for satisfactory therapeutic effect. When phenethicillin (6-(α -phenoxypropionamido)penicillanic acid) was marketed as "broxil," it was claimed that this preparation would give blood levels at least equal to those after intramuscular injection of corresponding doses of penicillin G. Knudsen and Rolinson (1959) investigated the absorption and excretion of phenethicillin in adults, and their results confirmed this claim. Garrod (1960) compared the antibacterial activity of phenethicillin, penicillin G, and penicillin V. He found that, weight for weight, phenethicillin was more active than penicillin V or G against resistant staphylococci, and very slightly less active against streptococci and pneumococci.

In February, 1960, an outbreak of severe pharyngitis, with some complications, occurred among schoolboys aged 7–13 at Summer Fields Preparatory School, Oxford. The school is residential, and it was essential to deal promptly with the infection, which spread in a few days to 31 boys. Table I shows the incidence of

TABLE I.—Clinical Diagnosis and Treatment

Condition	No.	Dose of Phenethicillin	Duration of Fever (Hours)	Failure
Pharyngitis due to β -haemolytic streptococci	13	{ 12–250 mg. q.d.s. 1–500 " "	{ 10–24 2–48	—
As above + otitis media	3	250 mg. q.d.s.	24	—
Pharyngitis due to other organisms	2	250 " "	{ 1–24 1–48	—
As above + otitis media	2	250 " "	48	—
Pharyngitis + bronchitis (2 β -haemolytic streptococci)	5	{ 2–500 mg. q.d.s. 3–250 " "	{ 4–24 1–48	—
Pharyngitis + sinusitis	4	{ 3–500 " " 1–250 " "	3–48	2, resistant staphs
Lobar pneumonia	1	250 mg. q.d.s.	73, with initial dramatic fall	—
Cellulitis of finger	1	250 " "	24	—

the various types of infection. Most of the boys had severe pharyngitis and cervical lymphadenopathy. The illness ran much the same course both in those infected with β -haemolytic streptococci group A and in those from whom other organisms (*Str. pneumoniae*, *Str. viridans*, neisseria) were isolated. Fourteen boys had complications. One boy had uncomplicated lobar pneumonia and one had cellulitis of a finger.

Methods

The boys were all treated with phenethicillin. The standard dose was 250 mg. (one tablet) four-hourly

during the day. In almost all cases there was a 12-hour interval during the night when no treatment was given. This dose was regarded as adequate for boys weighing 4½–7 st. (28.6–44.5 kg.). A few very big boys weighing 7–9 st. (44.5–57.2 kg.), and some with complications, were given 500 mg. q.d.s. Treatment was continued for five days in uncomplicated cases of pharyngitis, and for a week or 10 days in those with complications. The treatment was stopped in two cases (see Table I).

Blood for penicillin levels was taken once from each boy during treatment. The intervals between the previous dose of phenethicillin and venepuncture varied from 10 to 310 minutes. The concentration of antibiotic in the blood was determined by the tube-dilution method, using the Oxford H staphylococcus, and standard solutions of penicillin G and phenethicillin for comparison. The control solutions of penicillin G and phenethicillin gave identical results in every case.

TABLE II.—*Penicillin Levels in Blood*

Case No.	Age (Years)	Weight		No. of Doses of Phenethicillin Before Bleeding	Interval Between Previous Dose and Bleeding (Minutes)	Blood Penicillin (μg./ml.)
		lb.	kg.			
1	8	64	29.0	9	10	4
2	11	89	40.4	13	25	4
3	10	70	31.8	9*	30	2
4	11	71	32.2	17	40	2
5	12	81	36.7	5	40	4
6	8	66	29.9	5	50	8
7	12	106	48.1	9	65	4
8	9	71	32.2	7*	70	8
9	10	75	34.0	9	75	4
10	10	79	35.8	2	78	4
11	9	72	32.7	9	80	8
12	10	70	31.8	9	85	8
13	11	60	27.2	7	100	16
14	10	98	44.5	4	105	4
15	10	87	39.5	4*	108	16
16	10	66	29.9	4	185	2
17	9	67	30.4	4	190	1
18	12	110	49.9	3	195	0
19	9	63	28.6	4	220	1
20	8	62	28.1	4	220	0.25
21	11	66	29.9	4	230	0.5
22	8	64	29.0	4*	230	0.5
23	12	95	43.1	12	255	1
24	12	91	41.3	4	255	0.5
25	11	90	40.8	16	265	0
26	10	75	34.0	16	270	0.12
27	9	82	37.2	4	285	0
28	13	84	38.1	6	290	0
29	9	100	45.4	6	295	0
30	11	85	38.6	2	300	0
31	10	68	30.8	4	310	0

*These doses were 500 mg. All other doses were 250 mg. up till the time the blood was taken.

Results

The results are recorded in Table II, from which it will be seen that the blood level rises rapidly after taking the tablets, and drops again between three and four hours to very low or undetectable levels, regardless of the number of doses previously given. The absorption is obviously rapid, and the blood levels attained are comparable with those of penicillin G injected parenterally.

The clinical response to phenethicillin was very satisfactory. The patients with uncomplicated pharyngitis were afebrile and asymptomatic within 48 hours. The boy with lobar pneumonia responded as well as one would have expected had he been treated with penicillin by injection. The other complications cleared quickly (see Table I), except the cases of sinusitis. Three boys were afebrile within 48 hours, and symptoms settled after a further few days. Three boys did not respond to phenethicillin in a dose of 250 mg. four-hourly, and in two the fever remained high in spite of increasing the dose to 500 mg. q.d.s. From both, penicillin-resistant staphylococci were isolated, and they made rapid recovery when treated with erythromycin and

tetracycline respectively. Few objections were raised by any of the boys to the new drug. The prospect of not having to have injections (of which several boys had had previous experience) overshadowed the discomfort of one venepuncture for estimation of the blood penicillin level.

Side-effects.—Two boys complained of nausea soon after taking the tablets on an empty stomach, but this passed off after a few days. Three boys had diarrhoea; in two it was very mild, and in one who was receiving 500 mg. q.d.s. it was fairly severe, but it stopped when the dose was halved. In every case the diarrhoea ceased when the course of tablets was completed. One child was lethargic while receiving phenethicillin, but this ceased after treatment.

Summary

In a residential preparatory school an outbreak of severe pharyngitis affected 31 boys, 14 of whom had some complications. Group A β -haemolytic streptococci were isolated from most of the patients. All patients were treated with phenethicillin, and the clinical results were satisfactory. Blood levels of penicillin during therapy were equivalent to those expected from parenteral administration of penicillin G. Phenethicillin was rapidly absorbed, and concentrations up to 16 μg./ml. were obtained. The concentration fell to very low levels after four and a half hours.

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A TRIAL OF A NEW MONOAMINE OXIDASE INHIBITOR IN ANGINA PECTORIS

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Dramatic relief of angina pectoris with iproniazid (1-isonicotinyl-2-isopropylhydrazine; "marsilid") was reported by Cesarman (1957). Other early reports were also favourable (Cossio, 1958; Towers and Wood, 1958). The serious risk of liver necrosis from iproniazid later became recognized (*New Engl. J. Med.*, 1958), and recent double-blind trials have shown no improvement of angina (Dewar *et al.*, 1959; Snow and Anderson, 1959; Fife *et al.*, 1960). Iproniazid inhibits monoamine oxidase, and the alleged effect on anginal pain was ascribed to this action. As early enthusiasm for iproniazid has waned, other monoamine inhibitors have been tried in angina, and we here describe a double-blind trial of one of them.

1-Pivaloyl-2-benzylhydrazine ("tersavid") is chemically related to iproniazid. Animal experiments have shown equally powerful inhibition of monoamine oxidase, but it is less toxic than iproniazid. Relief of angina has been reported in preliminary trials.

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