Dr. Pugh then discussed the effect of cold on tissue temperature and blood flow. He showed that within 20 minutes of immersing the forearm in water at 17° C. the deep muscles cooled from 35° to less than 25° C., and the forearm blood flow fell from 3½ ml. per 100 g. tissue per minute to less than 1 ml. per 100 g. tissue per minute, in fact a mere trickle. He showed that the blood flow was not significantly increased by a sympathetic nerve block, and said that it was fairly well established that the blood vessels were directly sensitive to cold and constricted independently of impulses from the autonomic nervous system. The significance of this kind of work for rheumatology depended on the fact that the structures affected in rheumatic diseases were relatively superficial and therefore subject to the direct influence of changing environmental temperature.

There followed a number of clinical demonstrations. Dr. E. G. L. BYWATERS and other members of the staff of the Postgraduate Medical School of London showed a case of arthritis mutilans, a case of chronic post-rheumatic joint deformity of the type described by Jaccoud in 1867, and a case of parathyroid adenoma. Dr. E. DRESNER demonstrated a case of myeloid leukaemia associated with gout. Dr. L. G. C. PUGH discussed a case of Sjögren's syndrome in an elderly woman with rheumatoid arthritis, and showed with Dr. WILD a case of rheumatoid arthritis treated with ACTH. The remarkable subjective improvement in this patient on the third day of treatment was described. Methods by which it was hoped to secure evidence of the potency of the preparation and of its effects upon joint physiology and biochemistry were outlined, and a brief account was given of the general plan of the therapeutic trial.

Correspondence

R.M.B.F. Christmas Gifts—A Reminder

SIR,—I beg to remind your readers of the President's Christmas appeal (November 5, p. 1044), as the gifts are distributed before Christmas Day. All will acknowledge that the winter months are especially difficult and hard for old people living on small incomes. I therefore ask those who are willing to help the Fund in ensuring extra comforts and cheer to its elderly beneficiaries to forward their contributions as soon as possible, marked "Christmas Gifts," to the Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15.—I am, etc.,

London, S.W.15

C. LUTHER BATTESON,
Honorary Treasurer, Royal Medical
Benevolent Fund.

Resettlement of the Tuberculous

SIR,—Judging by recent correspondence in the medical press Professor Frederick Heaf (November 5, p. 1008) is not alone in thinking that the "tuberculous and non-tuberculous can be employed together without undue risk provided the non-tuberculous have overcome their primary infection, are adequately nourished, have a good standard of living, and work under hygienic conditions."

If the latter opinion is correct—and the experience of Papworth suggests that it may be so—it implies that before advising a tuberculous subject to return to industry it is necessary to: (1) Mantoux test and examine by x rays all his fellow workers; (2) persuade those who have a negative Mantoux reaction to work elsewhere; (3) provide the workers who remain with good food and houses; (4) make an accurate assessment of the hygienic conditions of the working environment and insist on the alterations necessary to bring these up to an unspecified "standard of goodness." A fifth requirement might be added—namely, that the patient himself should continue under regular supervision and keep strictly to the rules about coughing and disposal of sputum that are enforced in sanatoria.

The impossibility of achieving these objectives outside a well-organized tuberculosis colony is self-evident, and it is true it was realized that existing schemes for the resettlement of the

tuberculous in industry are potentially dangerous. These schemes have been devised to help disabled persons to make some contribution to production, but they overlook the possibility that it might be a national economy to keep every tuberculous subject in affluence rather than run the risk of their spreading the disease to fellow workers.

How great this risk is I had not myself realized until I had an opportunity of studying the tuberculosis experience of the shoemaking population in Northamptonshire. The results of this investigation have not yet been published in full, but in a preliminary report (May 28, p. 926) it was suggested that working conditions in boot and shoe factories facilitate the spread of the disease; that the presence of infectious persons in the working population leads to the development of new cases; and that in certain circumstances this mode of spread may treble the incidence of the disease. These preliminary findings are now supported by other evidence, which includes the following observation. During a survey of boot and shoe factories a mass-radiography unit examined 73 men who had been treated for pulmonary tuberculosis over five years previously and found that nine of them had signs of active disease. All nine were working at the time, none of them was under supervision, and five were shown to have tubercle bacilli in their sputum from a single examination by direct film. In two cases the interval between notification and mass radiography was over 20 years, and in four of the others it was over 10 years.

If, as seems likely, the findings in the boot and shoe industry apply to other occupations which suit the limited working capacity of tuberculous subjects it is clear that it is not safe for the tuberculous and non-tuberculous to work together in circumstances where strict supervision is impossible, and that we should cease quoting the experience of Papworth as evidence that it is so.—I am, etc.,

Oxford.

ALICE STEWART.

New Mechanism of Vitamin Deprivation

SIR,—I have read Professor P. Ellinger's letter (November 19, p. 1177) which refers to my paper on vitamin deficiencies in the sprue syndrome (October 1, p. 731). Professor Ellinger and his colleagues have shown that a relationship may exist between intestinal bacteria and the level of the urinary excretion of nicotinamide methochloride.¹ Professor Ellinger's observations do not provide a satisfactory basis for the understanding of the vitamin deficiencies observed in the sprue syndrome, for the following reasons:

1. Reduction of urinary nicotinamide methochloride cannot be regarded as a vitamin deficiency sign comparable to those observed in the sprue syndrome.

2. Professor Ellinger has described one case of nicotinamide deficiency following penicillin administration² and he quotes one other case following the administration of sulphadiazine.³ When one considers these two isolated case reports in relation to the hundreds of thousands of cases treated with sulphonamides or penicillin without any demonstrable vitamin deficiencies one is inclined to doubt the validity of Professor Ellinger's contentions.

3. The vitamin deficiencies in sprue may include riboflavin, pyridoxin, or folic-acid deficiency in addition to, alternating with, or in the absence of nicotinamide deficiency. A simple explanation such as the competition between nicotinamide-producing and nicotinamide-consuming bacteria⁴ will therefore not suffice.

4. Observations based on urinary excretion are of only limited value in the study of metabolism, and of even less value for the investigation of gastro-intestinal function. When these observations are made without regard to alimentary digestive changes, the chemical or physical state of the substance being absorbed, the route of absorption, or the destination of the absorbed material, their interpretation in terms of gastro-intestinal activity is likely to be unreliable. Professor Ellinger does not appear to differentiate between the administration of natural and synthetic vitamins or between their absorption from the stomach, the small intestine, the colon, the rectum, or the site of parenteral injection. The type of material absorbed and the site of absorption certainly makes a profound difference in the case of fats; it seems unwise to assume that they have no significance in the case of water-soluble vitamins.

In his letter Professor Ellinger makes four specific comments on my paper:

1. He contradicts my statement that the effect of antibacterial agents on vitamin deficiencies (in the sprue syndrome) is unknown.

In support he quotes the reduction of urinary aneurin¹ and nicotinamide¹ following administration of sulphonamides and the two isolated cases of true nicotinamide deficiency already referred to above.^{2,3} I was not referring to deficiencies caused by sulphonamides but to the possible effect of antibacterial agents on deficiencies already developed—as stated, this is at present unknown.

2. Professor Ellinger surprisingly questions my statement that nicotinic acid, riboflavin, pyridoxin, and folic acid are essential growth factors for bacteria, particularly those which are known to be present in the upper part of the small intestine in sprue. The organisms vary under different circumstances, but *Bact. coli* is not necessarily the predominating organism. The presence or otherwise of *Bact. coli* in no way affects the correctness of my original statement. Certainly *Bact. coli* can grow without these vitamins; certainly also *Bact. coli* can take up some of these vitamins and deny them to the host. Even if *Bact. coli* was the predominating organism in the upper intestine in some cases it would in no way invalidate the main arguments put forward in my paper.

3. Professor Ellinger misquotes me in his third comment. My original statement was that the part played by the intestinal bacteria in vitamin synthesis in normal human subjects is obscure. The observations quoted by Professor Ellinger were made in deprived subjects,⁴ or those treated with sulphonamides.¹ The significance of the vitamin synthesis by intestinal bacteria in normal subjects with a normal dietary intake is not clear. One of the reviewers⁵ quoted by Professor Ellinger writes: "The phenomenon of vitamin synthesis by bacteria presents important considerations in the nutrition of man. Its full significance, however, should await a more complete knowledge of the human need for the B vitamins than we now possess."

4. Professor Ellinger need not concern himself about my "main claim to have discovered a new mechanism causing vitamin deficiencies." I made no such claim. In my paper I have amplified and given the evidence in support of a suggestion which I originally made two years ago.⁶

Professor Ellinger further suggests that I am only reiterating his views on competition between different bacteria in the caecum. I trust that I have made it clear that this is not my suggestion and that I do not consider that any views so far put forward by Professor Ellinger and his colleagues provide an adequate explanation of the vitamin deficiencies in the sprue syndrome.

The essential point of my paper was to put forward the view that competition might occur between the bacteria and the host—similar to the competition that develops between the host and some intestinal parasites. Since there is usually an adequate supply of water-soluble vitamins in the diet in the cases studied, the overlapping of bacterial growth and the absorbing area in the intestine is implied. Professor Ellinger, however, summarily dismisses the question of bacteria in the upper intestine as irrelevant. His argument is that living *Bact. coli* take up nicotinamide; that dead *Bact. coli* release it; that *Bact. coli* are alive in the upper intestine, but dead in the rectum; that nicotinamide can be absorbed from the rectum; and, therefore, that the presence of bacteria in the upper intestine is irrelevant.

Professor Ellinger must be unaware that other organisms than *Bact. coli* are involved in sprue; that there are other deficiencies in sprue than nicotinamide deficiency; that there are absorptive faults in sprue which result in increased food supply for intestinal bacteria; that the bacteria in the fermenting sprue stools are often far from dead; that if bacterial growth is greatly increased vitamins may be released and taken up again by other bacteria; that the colon may be more quickly and more frequently emptied in sprue, which may interfere with absorption of released vitamins. It was only after careful consideration of the available evidence in relation to these facts⁷ that I put forward my suggestion that competition between the host and intestinal bacteria in the upper bowel might help to explain the vitamin deficiencies observed in the sprue syndrome.—I am, etc.,

Birmingham.

A. C. FRAZER.

REFERENCES

- ¹ Ellinger, P., Benesch, R., and Kay, W. W., *Lancet*, 1945, **1**, 432.
- ² — and Shattock, F. M., *British Medical Journal*, 1946, **2**, 611.
- ³ Hardwick, S. W., *Lancet*, 1946, **1**, 267.
- ⁴ Benesch, R., *ibid.*, 1945, **1**, 718.
- ⁵ Najjar, V. A., and Holt, L. E., jun., *J. Amer. med. Ass.*, 1943, **123**, 683.
- ⁶ — Johns, G. A., Medaury, G. C., Fleischmann, G., and Holt, L. E., jun., *ibid.*, 1944, **126**, 357.
- ⁷ — and Barrett, R., *Vitamins and Hormones*, 1945, **3**, 23.
- ⁸ Frazer, A. C., *British Medical Journal*, 1947, **2**, 641.
- ⁹ — *ibid.*, 1949, **2**, 769.

Pause for Réfection

SIR,—Dr. S. C. Dyke asks (November 19, p. 1179), "How and when is a rat 'refected'?" A rat is refected when a transmissible change in the intestinal content enables it "to grow and thrive without vitamin B in the food." The phenomenon was first observed by the late Professor L. S. Fridericia, of Copenhagen. He called it "refection," justifying his choice thus: "The phenomenon needs a name. We propose to name this restoring change 'refection' (Latin: *reficere* = restore)."¹ Professor A. C. Frazer (October 1, p. 731) was using a term now universally accepted to describe the condition.—I am, etc.,

Shinfield, Berks.

S. K. KON.

REFERENCE

- ¹ *J. Hyg., Camb.*, 1928, **27**, 70.

Hormones and Rheumatism

SIR,—I read with very great interest the important article by Professor Hans Selye (November 19, p. 1129) concerning the participation of the adrenal cortex in the pathogenesis of arthritis. It is perhaps a pity, in view of topical interest in the treatment of rheumatoid arthritis with "cortisone" and ACTH, that Selye writes about the effects of these substances on an experimentally induced arthritis. This must not be allowed to cloud a possibly much greater issue. It is not unlikely that other chronic lesions tend to perpetuate a vicious circle of "self-maintenance" by virtue of an adrenocortical effect. If this is the case, the results obtained with cortisone and ACTH in rheumatoid arthritis may well be eventually overshadowed by the effects of these hormones on many local and general chronic inflammatory lesions.

With these thoughts in mind, it would perhaps be best to regard Selye's "formalin arthritis" as a specific example of a chronic lesion rather than from the point of view of rheumatoid arthritis.—I am, etc.,

Newcastle-upon-Tyne.

A. L. LATNER.

Operative Treatment of Varicose Veins

SIR,—Mr. Harold Dodd has done a service in the fight against the varix by calling attention (November 5, p. 1046) to his results with the combined method of operation and sclerotic injection. At the moment some decry the use of sclerosants, especially at the time of operation, and call attention to the dangers of deep-vein thrombosis from their use. Mr. Dodd's figures, as do my own, prove that sclerosants do not cause this damage if used with discretion.

For several years I have attacked the varicose limb by means of a high resection of the internal saphenous vein (flush-tie), together with mechanical trauma to the venous intima in combination with the careful use of a sclerosant. My results over this time have been satisfactory and I have seen neither embolism nor damage to the deep veins. A follow-up of over 1,000 of my cases has satisfied me for the present at least that this is the most satisfactory method of attack. Varices in themselves are not a lethal complaint, and all forms of treatment must therefore carry a minimum risk.

The complex anatomical venous network is not accessible to the rough-headed needle, which is so useful in its destructive action on the main trunk. It is for these small radicals that the further aid of sclerosants is so valuable. The amount injected at the time of operation is important, and what is equally essential is that the sclerosant should be delivered in small divided doses as the traumatizing needle is withdrawn. Furthermore, immediately after operation both passive and active movements of the limb are essential.

The good results in these large series of cases are the best answer to those who deny themselves the advantage of sclerosants at the time of operation. It is to be hoped that others will publish their results, since it is by this method that progress will be made.

Mr. Dodd further states that elastic adhesive bandages should not be used in the treatment of varicose ulcers, and suggests alternative bandages. I cannot agree with this advice and am satisfied, as are most workers in this field of surgery, that the