Many Russians in my care during the war, even those who had been wounded before capture, awaited their return home with extreme terror. Why?

I agree that social security, whatever it may mean, has tended to reduce effort for the reasons advanced by Dr. Crichton-Miller. Many economists suggest that the economic basis for this social security is crumbling, so we may soon see the next phase developing.—I am, etc.,

Barnet, Herts.

G. C. PETHER.

Prognosis of Pleural Effusion

S.R.—Dr. Brian C. Thompson's reply to Dr. J. D. L. Reinhold's letter (Aug. 30, p. 348) prompts me to add my views on the point at issue in this important correspondence. A study of my cases in private and hospital practice during the last eight years goes to support Dr. Thompson's statement that "there was no evidence that differences in treatment of the original pleurisy affected the subsequent incidence of pulmonary tuberculosis." The study brings out two points conspicuously:

(1) The subsequent development of pulmonary tuberculosis is more common in those who show a "tuberculous diathesis." The latter can be recognized clinically to some extent from the history of tuberculosis in the family, relatively low weight, inelastic skin, dry hair, pallor, easy fatigue, "phthisical" configuration of the chest. Such persons are often styled by laymen as of "delicate constitution."

(2) Rest and sanatorium line of treatment have no effect on the prognosis. Under Indian conditions patients of pleural effusion, when afebrile and free from respiratory embarrassment, have to work with fluid still in the pleural cavity. They cannot afford to take rest till, as Thompson writes, "their blood sedimentation rate becomes normal." Under these conditions many have not developed pulmonary tuberculosis for over five years. Two female patients had one and two deliveries during this period, in spite of medical advice, without untoward effect. One patient who had effusion on one side and subsequently on the other is quite well and working now three years after.

This has been my impression based on clinical experience but unsupported by statistical data. I have come to believe that development of pulmonary tuberculosis subsequent to pleural effusion depends mainly on the "soil" and the resistance of the patient, to less extent on the environment and conditions of life of the patient, and to a negligible extent, if at all, on the rest and sanatorium treatment as held by Drs. Reinhold and Coope.—I am, etc.

Poona City, India.

P. L. DESHMUKH.

Early Diagnosis of Tuberculous Meningitis

SIR,—A patient was recently admitted for streptomycin treatment of a tuberculous meningitis only after he had been retained one week in another hospital because the chlorides in the cerebrospinal fluid (C.S.F.) had been found to be 0.72% and the diagnosis of tuberculous meningitis, to which other facts pointed, had consequently been rejected. A clear answer seems to be needed to this question: Given a patient with a meningitic picture whose C.S.F. shows a moderate pleocytosis, does a knowledge of the C.S.F. chloride level materially help to distinguish those cases suffering from tuberculous meningitis?

The chloride levels of the first specimen of C.S.F. examined in 52 cases of tuberculous meningitis, 8 cases of benign lymphocytic meningitis, and 10 cases of anterior poliomyelitis (all children) were as follows:

C.S.F. Chlorides	Tuberculous Meningitis Cases	Benign Lymphocytic Meningitis Cases	Acute Poliomyelitis Cases
0.70% or over ..	11	5	10
0.65–0.69% ..	23	3	—
0.60–0.64% ..	18	—	—
Total ..	52	8	10

It is seen that in 1 in 5 cases of tuberculous meningitis the C.S.F. chloride level was not lower than normal, while in nearly half the cases the chloride level fell within the zone of slight reduction (0.65–0.69%) in common with several of the cases of lymphocytic meningitis. In only a third of the cases of tuberculous meningitis was the chloride level substantially reduced

(0.60–0.64%), and in none did it reach the level of 0.59%, which is accepted as diagnostic of the condition. Thus, while a substantial lowering of the C.S.F. chloride level to 0.64% or less would, under the circumstances postulated, favour a diagnosis of tuberculous meningitis, the finding of a normal C.S.F. chloride level *should in no wise argue against tuberculous meningitis.*

All in all, I suggest that the time devoted by a clinical pathologist to an estimation of the C.S.F. chlorides would be more profitably spent in a search for acid-fast bacilli.—I am, etc.,

Newcastle-upon-Tyne.

DOUGLAS GAIRDNER.

Reiter's Syndrome

SIR,—As Reiter's syndrome occurs apparently mainly in young adults, I may be permitted to put the following case on record.

On July 23, 1945, an engineer, 55 years of age, consulted me for a purulent urethritis. No gonococci were found in the discharge. On Aug. 3, after 20 g. of sulphathiazole had been given, the discharge had practically ceased, and the smear contained only epithelial cells; but by that time the patient had a bilateral purulent conjunctivitis, again without gonococci in the smears.

On Aug. 10 the eyes were nearly normal, but he then had a painful swelling of an interphalangeal joint of the right foot, which took about 10 days to disappear. On Aug. 15 he started to complain of pain across the shoulders and in the lumbar region, without any obvious pathology, possibly due to a spinal arthritis.

He then went to his home in the North of England, and told me on his return that those pains did not leave him completely for more than two months. In the North a film of his spine was taken in which no changes were seen. He had no diarrhoea either before or during his illness.—I am, etc.,

Harrow Weald, Middlesex.

ALFRED LETCHNER.

Safer Administration of Intravenous Anaesthetics

SIR,—A method for increasing the safety in administering intravenous anaesthetics consists in giving the patient oxygen to inhale for two or three minutes before and during the administration of the intravenous anaesthetic. It is, in my opinion, particularly indicated in patients over 60 or ones who are sub-normal risks.

The rationale of this method is as follows. With most intravenous drugs given for anaesthetic purposes, and particularly with thiopentone, one is struck by the initial and severe depression of respiration that occurs. It is, I think, inevitable that some degree of anoxaemia must ensue, and it is this factor that endangers the patient. In many patients, particularly the elderly, in whom alarming symptoms are most likely to occur with these agents, there is the factor that their lungs have lost their full efficiency and that oxygenation of the blood is neither so quick nor so easy to bring about by the usual methods. If, however, one makes certain that the respiratory system is flooded with a high percentage of oxygen before this period of respiratory depression, then the period will do little harm.

In actual practice I have found that to all appearances my hopes have been justified; the patients have kept an excellent colour and there has been no cause for worry. Occasionally the patient has been told that "he won't have anything put over his face to put him to sleep"; then I assure him that what I am giving him to inhale will not put him to sleep but will help.—I am, etc.,

London, N.W.7.

D. C. CLARK.

Morphine in a Patent Medicine

SIR,—I should like to comment on the medico-legal note which appeared in your issue of Sept. 27 (p. 511), and referred to the death of a 2-year-old child after taking a patent medicine containing morphine. I gave evidence to the effect that the bottle when full contained just under 1 gr. (65 mg.) of morphine, but according to the *Daily Mail* (June 25) the manager of the firm which manufactures the medicine denied this, alleging that each bottle contained 0.432 gr. (28 mg.). In point of fact the incriminated bottle when full would contain 6 oz. (170 ml.) of fluid and as the concentration of morphine was 0.033% (as stated on

the label) this would work out at just under 1 gr., which is the amount I quoted in my evidence. I have had this checked independently by two chemists. I contacted the manager of the firm and he alleged that the *Daily Mail* had misquoted him. However, he told me that they have now suspended the sale of the preparation.

One further point. Your medico-legal correspondent refers to the Dangerous Drugs Regulations 1937 (S.R.O. 560), which allow the free sale of preparations, etc., containing not more than 2.5% of methylmorphine or ethylmorphine. This is correct, but surely does not apply in this particular case, as the medicine in question actually contained anhydrous morphine, so that the maximum concentration in an inert substance could not contain more than 0.2% in order to be sold freely to the public (*The Chemist and Druggist Year Book*, 1947, p. 339, para e).—I am, etc.,

Manchester.

PAUL B. WOOLLEY.

Dicoumarol

SIR,—In the annotation (Oct. 25, p. 662) on dicoumarol it is stated: "The prothrombin time is kept at one and a half times the normal value by means of daily doses of 100 to 300 mg. dicoumarol." Earlier it is stated that dicoumarol therapy should be continued for a month at least. Dicoumarol is a very valuable drug, very effective and quite safe if carefully controlled. However, to recommend that 100 mg. to 300 mg. should be given daily for at least a month—even with daily prothrombin estimations as controls—is courting danger.

It would be much safer to recommend 300 mg. a day for two days, then wait for the prothrombin time to lengthen and give no more dicoumarol until the prothrombin time has shortened nearly to normal; this may take ten days. The renewal dose of dicoumarol may be quite small, 25 mg. or 50 mg., and the reaction to the renewal dose will be much greater and more rapid than to the initial doses. There is danger of discrediting a very useful remedy unless dicoumarol is used with great care.—I am, etc.,

Epping, Essex.

FRANK MARSH.

SIR,—The annotation on dicoumarol (Oct. 25, p. 662) prompts me to make certain points which would appear to be of vital importance to those proposing to use that drug.

(1) With levels of dosage of dicoumarol similar to those mentioned by your annotator a sharp rise of the prothrombin time is seen to occur at any time between the 12th and 24th days of therapy. If therapy is discontinued at this time, it is my experience that the prothrombin time not only takes three or four days to fall to safe levels, but may rise alarmingly during those days. It would appear that a cumulative effect of the drug occurs, an effect which constitutes the main danger of dicoumarol, for it is impossible to prognosticate how high the prothrombin time will rise in any given case. It is surprising that more is not made of this cumulative effect in the British or American literature.

(2) Your annotator states that haemorrhagic manifestations may be treated with 50 to 100 mg. of vitamin K intravenously or with blood transfusion. A case of my own was under treatment with dicoumarol for post-operative venous thrombosis; 300 mg. were administered on the first day followed by 100 mg. daily. After nine days' treatment the dicoumarol was discontinued, as the prothrombin time had reached 32 seconds. In the next six days one 50-mg. dose of the drug was given to prevent a return to more normal levels of the prothrombin time. This dose should not have been given, as there were red cells in the urine. Six days after the end of the main course, and three days after the 50-mg. dose, the prothrombin time reached 46 seconds and severe haematuria developed. Vitamin K was administered on this day and for the following five days, at a rate of 150 mg. orally per diem. On the first two days of vitamin K therapy 1 pint (568 ml.) of blood was administered. Haematuria remained profuse for two days, diminished on the third day, and was absent from the fourth day. The prothrombin time did not fall until the fifth day, when it fell abruptly to 22 seconds and thereafter to normal levels. This experience strongly suggests that those using dicoumarol should bear in mind that a rapid response to vitamin K and even blood transfusion cannot be counted upon when dicoumarol therapy has produced dangerously high prothrombin times.

(3) Your annotator states that the prothrombin time should be kept at one and a half times normal during dicoumarol therapy. As Allen¹ has shown, it is not adequate to control the therapy by prothrombin times alone. Allen has shown that venous thrombosis is unlikely to occur if the prothrombin percentage is less than 30% of the patient's normal and that 10% of the patient's normal is the critical level for haemorrhagic manifestations. The control should be by prothrombin percentages, which can be obtained from the prothrombin time by the method described by Allen. The margin of safety in dicoumarol therapy is so narrow that any attempt to simplify the control methods is liable to be fraught with grave danger and should be regarded with grave misgivings.—I am, etc.,

Mauchline, Ayrshire.

GAVIN CLELAND.

REFERENCE

¹ Allen, E. V., *Quart. Bull. Nthw. Univ. med. Sch.*, 1946, **20**, 1.

Nicotinamide and Blood Sugar

SIR,—I have been interested in the recent article by Dr. J. N. Cumings (Oct. 18, p. 613) on nicotinamide and blood sugar, in which he refers to investigations carried out by me in 1943. It is indeed surprising that such discrepancies in experiments and medical observation can arise, but in Dr. Cumings's work it is certain that many well-established observations on the action of insulin have been overlooked. It is always difficult to adjust curves so that they start from the same level, but in this particular investigation care should have been taken to start from a lower level, for it is well known that the higher the blood sugar the greater the action of insulin. The latter is naturally taken as the deciding factor in the abstracting mechanism of sugar from the blood. The similarity of the curves obtained suggests that the relationship between nicotinic acid amide dosage and its effect was of the same nature in all four subjects. What has not been taken into account is the nature of those factors which so uniformly modified the results in contradistinction to my own.

One may regard the action of nicotinic acid amide by analogy with insulin as the resultant of two opposing forces—viz., the action of the sugar-abstracting mechanism and the glycogenolytic mechanism liberating sugar into the blood. If a level of 105 mg. % is regarded as the uniform fasting level of all individuals tested, then there is after half an hour an abstraction of sugar of 12 mg. %. After one hour there is a rise in the curve by the addition of 5, after one-and-a-half hours of another 5 mg. %, and at the end of two hours sugar is again abstracted from the blood by 14 mg. %. Thus in Cumings's curves, where the fasting level is high, the first sign that the fall of blood sugar is opposed is shown (probably in all four experiments) by a rise in blood sugar after one to one-and-a-half hours, a sign that the raised activity of a surplus of insulin is at once masked and counteracted by a compensatory supply of sugar from the liver into the blood. Otherwise why should there be first an abstraction and then an addition of sugar? For this reason all subjects should have been allowed to settle to a more physiological fasting level on a strict diet before experiments started. It is also suggested to compare the results of smaller doses of injected nicotinic acid (not nicotinic acid amide) and ingested nicotinic acid amide—i.e., 100–300 mg.—to avoid if possible, or to lessen the reaction of, the opposing mechanism. Individual reactions to nicotinic acid vary as they do with insulin, and before larger doses are given smaller ones would ascertain individual reactions to the drug.

The practical value of nicotinic acid in certain cases of elderly diabetics is in my opinion unequivocal, and every case should be first tested as to its response over a period of one to two weeks in varying doses before any other measures are resorted to.—I am, etc.,

Rochdale.

F. J. NEUWAHL.

SIR,—I was very much interested in the article by Dr. J. N. Cumings (Oct. 18, p. 613) and in his negative findings of the effect of nicotinamide (N.A.A.) on the blood-sugar levels in normal controls and in diabetic patients. In spite of these negative findings I feel that there is something in this subject that has not yet been explained, and my clinical experience of two cases in which there has been without doubt some benefit