Correspondence

Haemoglobinometry

SIR,—Martindale in the *Extra Pharmacopoeia* remarks, "Although the determination of the amount of haemoglobin is one of the most important of all the chemical tests of the blood, yet as a rule it is one which is determined with less care and by methods more inaccurate than those in use for any other constituents of the body." Most people, I imagine, will agree with this statement.

The two common methods in general use are the Tallqvist scale and Sahli's instrument. The Tallqvist scale is useful in giving an approximate idea of the degree of anaemia and in following the progress of a case under treatment. Few, however, I imagine, would use it for calculating the colour index or (what is perhaps more definite) in distinguishing between macrocytic and microcytic anaemias, the calculation of the mean corpuscular volume and the mean corpuscular haemoglobin content. Outside the laboratory the Sahli instrument is more commonly used for this. The Sahli instrument, of course, depends on the alteration of the haemoglobin to acid haematin. The change of colour here is continuous. About 95% of the change is attained in 10 minutes and it is finally complete in about 40 minutes. And here it seems to me that we get into difficulties.

For some time now, in estimating the colour index or the mean haemoglobin corpuscular content, I have wondered if my results were just what they ought to be. Sahli, in his original description of his instrument in *Diagnostic Methods* (1907), advises: "as soon as the mixture approaches a dark brown colour water is added." The Standing Committee on Laboratory Methods of Glasgow University advises in italics "exactly one minute." The makers of my instrument (Leitz) advise "shaking the tube for one minute and setting aside for 1 to 2 minutes before diluting." Whitby and Britton, in *Disorders of the Blood* (1939), advise a wait of 30 to 40 minutes before diluting. The graduation of my instrument in regard to the quantity of haemoglobin in grammes per 100 c.cm. of blood is the same as that shown diagrammatically in their book. I have made a few estimates with different patients, using first a 2-minute interval before diluting and repeating the experiment after waiting 40 minutes. The average reading after 2 minutes was 76% and for 40 minutes 94%, an average difference of 18%. In view of the above the Sahli method seems to me somewhat unsatisfactory. I have been using a Lovibond comparator with colour disks to compare with undiluted blood in a thin film in a special blood cell. This is graduated according to the Haldane scale, and in its lower ranges should give a closer approximation than the Tallqvist scale. This is a very handy instrument, but I find it difficult to get a close approximation, due possibly to the comparison between a clear glass and a suspension. Tintometer, Ltd., also make colour disks for the Haldane method and the acid haematin method. Incidentally, in the latter they allow 40 minutes for the final change of colour. These may be better than the undiluted blood method, but I have not tried them.

The main desideratum in the estimation of haemoglobin by colorimetric methods is that the change of colour should be rapid and complete. This might be accomplished by nitrites or other reagent giving a change to methaemoglobin, but I think the best solution is the Haldane method. I notice that Cecil Price-Jones in his book *Blood Pictures* mentions Haldane's method alone. To-day, of course, the difficulty with the Haldane method is in obtaining the necessary supply of coal gas. This difficulty, I think, could be overcome by the "sparklet" method. The quantity of carbon monoxide required is not large, so the sparklets could be small. The apparatus for releasing the gas could also be made small enough to go in a case without making it unduly bulky. With this and two standards, one for daylight use and one for artificial light, I think one would have a haemoglobinometer much more satisfactory in its results than the Sahli instrument.

These remarks are made from the viewpoint of the general practitioner and take no account of the more accurate methods used in laboratory technique.—I am, etc.,

Kirriemuir, Nov. 5. ROBT. D. CAMPBELL, M.B., Ch.B.

Fate of the Blood Lymphocyte

SIR,—In his review of *Lymphatics, Lymph, and Tissue Fluid*, by Drinker and myself (November 8, p. 653), your reviewer does me the honour of quoting verbatim some of my views on the defence function of the lymphatic apparatus, but has misrepresented somewhat my views on the fate of the blood lymphocytes. He states: "Yoffey thinks they go to the bone marrow to be the precursors of the red cells and granular leucocytes, but his arguments are not altogether convincing." Actually, while I believe that, on balance, the admittedly conflicting evidence at present available inclines to this view, it is far from proven. It certainly has not been proved to my own satisfaction, as indicated by several passages in the book, of which perhaps I might instance the following (p. 274): "The most careful histological studies of bone marrow have yielded inconclusive results, and the problem will probably not be solved to the satisfaction of everyone until new experimental lines of attack have been devised. If, for example, one could mark the lymphocytes by means of a vital stain, it might be feasible to collect a large number of lymphocytes in thoracic duct lymph, stain them, and reinject them into the blood. Examination of the bone marrow some hours later would show whether any of these marked lymphocytes had reached it. Possibly the statistical study of lymphocyte development used by Kindred (1940) may be further utilized."—I am, etc.,

Department of Anatomy, University of Bristol, Nov. 11. J. M. YOFFEY.

Dark-adaptation Tests and Vitamin A Deficiency

SIR,—Since many workers are using studies of dark adaptation as a means of detecting deficiency of vitamin A, it seems undesirable to allow the conclusions of Dr. E. Wittkower and his collaborators (October 25, p. 571, and November 1, p. 607) to pass unchallenged. In a group of admittedly psychopathic soldiers who complained of night-blindness they found only about one-third with subnormal dark adaptation. Arguing that the diet of these men must have been adequate in vitamin A, they conclude that "the value of dark-adaptation tests for the discovery of night-blind patients and as an indicator of vitamin A deficiency appears doubtful." This statement is clearly open to several important criticisms, which may be summarized as follows:

1. There is no doubt at all that poor dark adaptation is in fact associated with vitamin A deficiency. (*a*) Experimental diets deficient in vitamin A result in defective dark adaptation, which is reversed when the vitamin is taken. (*b*) Poor dark adaptation is commoner among individuals from the lower-income classes. (*c*) In almost all instances such poor dark adaptation is improved by the administration of vitamin A. To state, as do Dr. Wittkower and his colleagues, that the diet of their subjects was adequate in vitamin A is surely begging the question. It has been shown by numerous investigators that apparently normal diets are frequently not adequate in this vitamin, and that many individuals consuming them show poor dark adaptation which is cured by the administration of vitamin A.

2. A more serious criticism, however, is that the conclusions of Dr. Wittkower and collaborators are based on a *non sequitur*. They find that subjects suffering from severe psychological disturbance may complain of night-blindness, and that this may or may not be accompanied with demonstrably defective dark adaptation. Thus, they argue, the test cannot be used for the detection of deficiency of vitamin A. In other words, psychopathic individuals may show diminished powers of dark adaptation, and hence the measurement of this would probably detect mental instability rather than vitamin A deficiency. An analogy might perhaps best demonstrate the invalidity of this argument. A hysterical patient complains of defective vision or hearing. She finds it impossible to see the test type or to hear the ticking of a watch. Are we then to conclude that such visual or auditory tests cannot be used for the detection of organic blindness or deafness?

Subjective tests such as those for dark adaptation are, of course, dependent to a large extent on the co-operation and mental state of the individual being tested, and no one would deny the importance of bearing this in mind. The paper by

Dr. Wittkower and his co-workers serves a useful purpose in drawing attention to the psychological aspects of tests for night-blindness. In so far, however, as it attempts unwarrantably to minimize the usefulness of such tests for the nutritional worker, it is to be deplored.—I am, etc.,

Dunn Nutritional Laboratory, Cambridge, Nov. 7. JOHN YUDKIN.

Blood Transfusion and Syphilis

SIR,—The number of persons now receiving blood transfusion is increasing due both to war conditions and also to a natural extension of the practice. The transmissions of syphilis by this means are, as at present recorded, relatively very few, but there may be more cases not reported for obvious reasons. Further, it would seem that war conditions have increased the number of persons suffering from syphilis.

The risks would lie in two classes of blood transfusion: (1) that of whole blood immediately used, and (2) perhaps in stored whole blood used early. The Wassermann, or any other serological safeguard, cannot entirely eliminate the risks of transmission. There might be, for instance, cases (*a*) where the person tested is incubating the disease, (*b*) where a chancre is present but the case is in an early sero-negative stage, and (*c*) where a person has acquired the disease after being tested and prior to being called upon to give his blood. The expense and time consumed in serological tests are considerable. The administration of whole blood practically immediately after withdrawal from the donor would be, in an infected donor, a very grave matter, especially in the early stages of syphilis referred to above, and in which the serological tests might be negative during the septicaemic stage.

In regard to stored blood it is a fact that *Treponema pallidum* is stated to be able to survive for considerable periods in various materials from infected persons and animals. Reference to Volume 8 of the *System of Bacteriology* will give some data on this matter. We do not know of any work which has been conducted on the survival of *Treponema pallidum* under refrigerator storage conditions.

From the above considerations it appears to us that the work of Kast, Peterson, and Kolmer,[1] and especially a recent publication by Eichenlaub *et al.*,[2] are of premier importance. The latter group of workers used mapharsen to rid infected citrated blood of *Treponema pallidum*. They found that 0.01 gramme per 500 c.cm. of citrated blood was amply sufficient for the purpose, and based this finding largely on work on rabbits which were exposed to infected material without the addition of the arsenical mapharsen. Mapharsen is of relatively low toxicity, and, in the amount suggested, the dose is so small as to be most unlikely to affect even a very seriously ill person. Further, the drug is directly antitreponemal and does not require chemical action to form arsenoxide. Contraindications might arise in cases where the recipient was suffering from (1) haemorrhagic purpura, (2) exfoliative dermatitis, (3) hepatic disorders, and (4) renal disease. The cost of sterilizing against *Treponema pallidum* in 500 c.cm. of citrated whole blood would be relatively small.

While in no way claiming to possess any expert knowledge in regard to blood transfusion, the method advocated by Eichenlaub and his collaborators would appear to us to add yet another safeguard to the recipient of a blood transfusion. We venture cordially to congratulate the above workers, and also to suggest that the value of the method shall be considered by those more qualified than ourselves to judge of its practicability and utility.—We are, etc.,

H. A. COOKSON, M.B., F.R.C.P.Ed.
November 10. W. GILLIES ANNAN, M.D., F.R.C.S.Ed.

Possibility of Malaria in Britain

SIR,—Dr. I. F. Mackenzie's letter (November 8, p. 668) is a timely reminder to general practitioners and those temporary Service medical officers who have little or no experience of malaria. As a result of the technique of investigation, treatment, and control evolved since the last war, I think it would be fair to say that there is less risk of oversight on the part of regular medical officers of all Services.

Malaria is a potential danger wherever "carriers" and anopheline mosquitoes coexist, but certain areas were especially dangerous in the last war. Cases of indigenous malaria have occurred in certain areas after every war in which troops have been exposed to infection over-seas, and the present war will probably be no exception. Thanks to the knowledge with which we are now armed, and given early diagnosis and efficient treatment of indigenous cases, there is little danger of the latter ever reaching serious proportions.

The following table is taken from *Observations on Malaria* (H.M.S.O., 1919):

Carriers of Malaria under Treatment during May to September, 1918

1918	Sheppey		Lydd		Sandwich	
	In Hospital	Not in Hospital	In Hospital	Not in Hospital	In Hospital	Not in Hospital
May	—	491	12	74	13	7
June	—	552	7	84	14	18
July	—	550	Nil	24	10	47
August ..	—	349	1	23	8	17
September ..	—	46	1	33	6	32

The above figures relate to men from over-seas. During 1918 sixty-one cases of indigenous malaria in serving soldiers were reported. Each case was carefully investigated; none had a previous malarial history and most of them had never been out of this country. The indigenous character of the infection was established in every instance. Forty-two cases occurred in the Sheppey, Isle of Grain, Sandwich, and Lydd areas, and the remaining nineteen were distributed between Aldershot (4), Suffolk (6), Norfolk (2), Essex (2), Sussex (1), Leicester (1), Notts (1), Lincs (1), and Herts (1). Twenty-nine foci of infection were located.

References to "ague" in the literature of the sixteenth century make it clear that malaria was endemic in England at that time. It is now practically, if not quite, extinct, not because of any sanitary measures specifically designed for its eradication, but as a fortuitous result of the improvement in the general sanitary condition of the country.

Introduction of a natural reservoir of infection in the form of malaria patients from over-seas certainly supplies what Dr. Mackenzie calls "the missing link"; but Service authorities are fully alive to the risk to the civil population thereby entailed, and every care is taken to render patients parasite-free before they are "turned loose" on the uninfected anopheline. It must not be forgotten that even in peacetime there is a continual traffic of infected civilians on leave from over-seas, who are usually far less carefully supervised.

It is doubtful whether medical officers of health do all they might to discover and eradicate anopheline breeding-places. I have in mind certain stagnant pools and miles of derelict canals which I have myself dipped and proved to be prolific nurseries of anopheline larvae.—I am, etc.,

Brookwood, Nov. 9. H. M. STANLEY TURNER.

"Euglamide" in Treatment of Burns

SIR,—In the *Journal* of March 29 (p. 469) we reported the results obtained in burns treated with a glycerin sulphonamide paste termed "euglamide." Briefly these results appeared to indicate that the use of the paste led to prompt healing and that it might be of value in the treatment of third degree burns and in burns of the hands and face. Work on this subject has been continued, and we have made several alterations in the dispensing, though the principle of using a water-soluble sulphonamide in glycerin has been retained.

(1) Work which one of us (J. M. R.) has carried out in collaboration with Major G. I. Scott has shown that a solution of sodium sulphacetamide (supplied in a 30% solution by British Schering Ltd.) exhibits a much higher chemotherapeutic activity than a similar solution made by dissolving the solid material (supplied by the same firm) in water. For this reason we now use the 30% solution in making up the euglamide.

(2) By making up the paste with "eucerin" (a proprietary ointment base made from the oxycholesterin of wool fat and

[1] *Amer. J. Syph. Gon. ven. Dis.*, 1939, **23**, 150.
[2] *Arch. Derm. Syph.*, 1941, **44**, 441.