have never yet come across a purely anatomical textbook which describes any vesico-uterine ligaments other than the utero-vesical folds of peritoneum.—I am, etc.,

E. Hesketh Roberts, F.R.C.S.Ed.

London, W.1, Dec. 12th.

Hookworm Infection

Sir,—In the *Journal* of September 10th there are two communications on hookworm disease.

The first is a report on a case of hookworm disease by Dr. W. M. Fallon (p. 515), in which the remarkable points are: (*a*) a haemoglobin of 85 per cent. and a leucocyte count of 26,600, with 75 per cent. eosinophils; (*b*) what the patient felt "was an attack of asthma, which lasted three weeks"; and (*c*) symptoms to be summarized as lassitude and irritability.

The second is a letter from Dr. Harper (p. 535), which ascribed to hookworm infection two conditions: (*a*) polyarthritis with high fever and a general resemblance to acute rheumatism; and (*b*) a tendency to haemorrhage from small arteries and capillaries. As comment on Dr. Harper's remarks on the prevalence of acute rheumatism in Fiji there is a letter from Dr. J. T. Clarke in the *Journal* of October 1st (p. 650), in which he stresses the accepted rarity of acute rheumatism in the Tropics.

I seek to suggest another explanation of the above three conditions. It has crystallized out of numberless correlations of clinical and laboratory findings.

1. That heavy hookworm infections only occur where, as the result of achlorhydria, the first part of the duodenum is continuously of high alkaline *p*H.

2. That the achlorhydria is resultant on lowered alkali reserve of the plasma, and thus of altered chemistry in the formation of hydrochloric acid. This lowered plasma bicarbonate is the first and continued result of bacterial toxaemia from the small bowel.

3. The commonest bowel infections in the Tropics belong to the Flexner and post-Flexner groups. It is their attack on the small bowel, causing entero-dysenteric symptoms in infinite variety, which arouses the immunity forces of the body into a long-drawn battle.

4. That the high haemoglobin and great eosinophilia are an evidence of high immunity against this group. It was, as it were, rather developing than developed—hovering between allergy and immunity and being hindered by the persistent hookworm. The supposed asthma attack I would interpret as an activity of the sympathetic member of the immunity chain.

(I would further submit: (*a*) That the lassitude and irritability symptoms were due to the lowered plasma bicarbonate affecting the adrenal-sympathetic system, and that, had the patient been treated with adequate alkali, as the alkali reserve rose these symptoms would have yielded to those of well-being; (*b*) also that, as a presumed achlorhydria recovered on the alkali treatment, with hydrochloric acid return the hookworm would have died out spontaneously. I have very frequently seen this happen.)

5. That the polyarthritis with high fever is an immunizing process involving mesothelial cells. It is of high value against Flexner groups, and seems to confer recovered health, which is well sustained.

6. In a large out-patient and village work, as well as in the wards, I habitually consider the possibility of Flexner infections being a cause of menorrhagia, repeated abortions, and purpuric conditions. Hookworm may or may not be present also.

—I am, etc.,

Flora R. Innes, M.B., Ch.B.,
Lecturer in Medicine and Physician in Charge of Medical Department, Medical School for Women, Vellore, S. India.

November 14th.

Tuberculin in Diagnosis

Sir,—Professor Lyle Cummins, in his contribution to the Centenary Meeting (*British Medical Journal*, December 17th, p. 1089) has overlooked the advantages of the subcutaneous tuberculin test, to which I should like to refer.

The cutaneous tests are qualitative, revealing the existence of tuberculous infection without any definite indication as to whether infection is latent or active. Various attempts have been made to make the cutaneous test quantitative, but without success. There is not only the incalculable factor of the amount of tuberculin absorbed by the skin, but also the difficulty of measuring accurately a small area of induration. The intracutaneous test is more accurate, but, as Dr. d'Arcy Hart has pointed out, the diagnostic value of a positive reaction, except in children under 5 years of age, is diminished by the fact that of 751 clinically non-tuberculous controls, 40.5 per cent. gave a positive reaction, and that of 134 adults in this group 95 per cent. gave a positive reaction. This makes a negative reaction of great diagnostic value in excluding tuberculous infection, but apparently there is only a 5 per cent. chance of obtaining a negative reaction in the hospital class of patients from which these controls were drawn. The subcutaneous test overcomes these difficulties. It is not only qualitative but also to a large extent quantitative. Within limits it reveals not only the presence of tuberculous infection, but also whether that infection is latent or active. In this test we seek to provoke a febrile reaction which is easily recognized. Apart from moribund cases, and cases of miliary tuberculosis or of meningitis, in which all response is abolished, it appears that the greater the reaction and the smaller the provocative injection, the more active is the infection. At the other end of the scale the smaller the reaction and the greater the provocative injection the less active is the infection and the greater the immunity.

When tuberculosis is suspected, without tubercle bacilli in the sputum, I do a cutaneous test by the tattoo method with pure old tuberculin. If that is negative active infection can be excluded, and in all probability latent infection likewise. With a positive cutaneous test I proceed to the subcutaneous test with a view to discovering the degree of activity or of latency of the infection, and the need for immunization by tuberculin treatment. A febrile reaction to 0.0001 c.cm. of old tuberculin is evidence of active tuberculosis, whereas no reaction to 0.01 c.cm. excludes active tuberculosis. This is not a mechanical method of diagnosis, because around reactions to 0.005 c.cm. there is a no-man's land, where every other factor in the case must be weighed equally in the balance.

In skilled hands there can be no more risk with the subcutaneous than with the intracutaneous test. In both these tests tuberculin is injected into the system. With the intracutaneous test the absorption of tuberculin is slower but no less sure, and the intracutaneous test may provoke not only febrile but also focal reactions. In point of fact, a general reaction may follow a von Pirquet or even a Moro test.

Professor Lyle Cummins has said that "for purposes of diagnosis in man the tuberculin test in all its varieties is definitely inferior to the combined radiological, physical, and laboratory examinations which have come to be the routine methods." The routine laboratory test is sputum examination, but the presence of tubercle bacilli in sputum is not a sign of early pulmonary tuberculosis, nor does their absence exclude the presence of tubercle. Again, the physical signs of early pulmonary tuberculosis are not diagnostic, and may occur in other conditions of the lung. With radiography a tuberculous nodule must attain a size of 4 c.mm. before a shadow is thrown, and whilst increased striation, especially at the apices, is suspicious, it is not diagnostic. To stress this point I have collected from my

records eighteen cases in which no tubercle bacilli were found in the sputum, in which I was unable to detect any abnormal physical signs in the chest, and in which the radiogram showed nothing more than increased apical striation. By the subcutaneous tuberculin test, in conjunction with symptoms, I diagnosed ten of these cases as tuberculous and eight as non-tuberculous. The non-tuberculous cases included neurasthenia, emphysema, post-pneumonic fibrosis, gastritis, and post-malarial debility. In this group of cases the diagnosis, such as it was, was more accurate by reason of the subcutaneous test, and in the diagnosis of early tubercle in lungs, glands, or elsewhere the subcutaneous test is superior to "the routine methods," and is indispensable.—I am, etc.,

London, W., Dec. 17th. HALLIDAY SUTHERLAND.

Dosage of Tuberculin

SIR,—In the paper on "The position to-day of tuberculin in treatment," read by Dr. R. A. Young in the Section of Tuberculosis at the Centenary Meeting of the British Medical Association, and published in the *Journal* of December 17th, a scale of dosage is laid down which is usually followed by the author. This scale is so irrational that I am not surprised that Dr. Young regards the danger of tuberculin treatment as considerable. To show the absurdity of Dr. Young's scale one need only set down his succession of doses, placing opposite the percentage increase of each dose over its predecessor, thus:

1/500,000 mg.	
1/400,000 mg.	Increase 25 per cent.
1/300,000 mg.	Increase 33⅓ ,,
1/200,000 mg.	Increase 50 ,,
1/100,000 mg.	Increase 100 ,,

Dr. Young then says: "After this the doses can be more rapidly increased." After which he gives:

1/75,000 mg.	Increase 33⅓ per cent.
1/60,000 mg.	Increase 20 ,,
1/45,000 mg.	Increase 33⅓ ,,

and so on.

The proper way to use tuberculin is to begin, as Dr. Young does, with a very small dose; and, if this produces no apparent reaction, to increase by 100 per cent. increments till some reaction is produced. This dose should be repeated without increment till it can be tolerated without apparent reaction. Or, if the reaction first produced be severe, the dose should be reduced somewhat. Then one should find by trial the highest rate of increase that can be tolerated without producing reactions, and adhere to that. This rate is very different for different people. In some cases only about 10 per cent. increases can properly be given; in others a much larger rate can be used. In one or two cases I have given 70 per cent. increases over a long period with advantage. I drew attention to the absurdity of Dr. Young's scale of doses at the time, after he had read his paper. Dr. Young's reply to my criticism was that he was not a mathematician. I say that anyone who does not know enough elementary mathematics to follow the method I have outlined should not venture to give tuberculin. Nor should he, because it would be dangerous for him to use it, consider that it is dangerous when administered by those who know how to use it aright.—I am, etc.,

Belfast, Dec. 17th. JOHN R. GILLESPIE.

SIR,—As I had no opportunity of seeing Dr. R. A. Young's address before it was delivered, I hope you will allow me to comment upon it as it appears in your columns to-day. As a medical man who has used tuberculin in diagnosis and treatment without a pause for more than forty years in all forms of chronic tuberculosis, especially in chronic phthisis, with outstanding success, that can be proved by a simple reference to records published first in 1909 and extending up to to-day, I must protest against Dr. Young's first sentence: "The introduction of tuberculin was one of the greatest tragedies of medical research." I am ready to meet Dr. Young on any platform and vindicate the transcendent value of tuberculin both in diagnosis and in treatment, if tuberculin be used in the right way, in right doses, at the right intervals and in the right cases, and with a clear conception of the conditions and limitations laid down by the great master himself. In my last interview with Robert Koch in 1909 we discussed dosage. I told him that 0.6 c.cm. of the stronger tuberculins was the minimum dose to achieve any great success by specific treatment in the commonest of all forms of tuberculosis—chronic phthisis, which is the essential source of more than 90 per cent. of all forms of tuberculosis in man. Professor Koch at once replied: "Indeed, that is interesting; we have found that in animal experiments a dose of 0.5 c.cm. is necessary to develop the phenomenon of complement-fixation."

Dr. Young's dosage is useless; it cannot develop any degree of immunity. By Arneth's test I have demonstrated, even to pupils of Sir A. Wright, that only large doses of tuberculins of various sorts can bring about a reversion of the leucocytes to the normal type in the blood (see charts in my Weber-Parkes prize essay). I can assure the medical profession, though I may not convince Dr. Young, that such doses as Dr. Young uses as his final dose cannot have the slightest effect in producing any favourable result in the treatment of any open form of chronic phthisis. His system of dosage is quite out of harmony with that which I have been using for many years every day in the treatment of all forms of chronic tuberculosis.

Recently an investigation upon the value of tuberculin in advanced cases of chronic phthisis has been carried out by Dr. James Watt. Whatever may be the result of that investigation it has been proved that large doses alone can benefit the sufferer. In all the cases in which improvement has been noted large doses have been used—mostly 1 c.cm. or more T.A.F. and 1 c.cm. or more B.E. I would ask Dr. Young why he persists in measuring the doses in such a way that few, if any, can understand them. He says he begins with 1/500,000 mg. and ends with (at most) 1/500 mg. As he used old tuberculin (T.A.), I should like to know how a fluid can be weighed each time. There is certainly no known quantity of solid substance in T.A. I am forced to the conclusion that the doses have not been measured by Dr. Young, but by an expert, probably the bacteriologist. If there is one thing that is a *sine qua non* in specific treatment it is that the dose must always have a relation to the previous dose, and must be prepared by the physician on the spot. I have always measured each dose myself. The amount of the dose should, and must be, described in terms of fluid, and not solid, measure. Any medical man may see for himself the evidence that proves the value of methods based entirely on Koch's discovery of tuberculin if he will visit my clinic, 11, Nottingham Place, W.1, any Monday or Friday afternoon.—I am, etc.,

W. CAMAC WILKINSON, M.D., F.R.C.P.

London, W.1, Dec. 17th.

"Excitability: A Cardiac Study"

SIR,—The couple of paragraphs by your reviewer did scant justice to the book on excitability by Professor Burridge. As in the case of other original thinkers, Burridge has met with difficulty in the publication of his research work, because it ran counter to the received opinion of physiological pundits. Starting out with the