Efforts are being made along a number of different lines to discover some blood reaction which will assist in the diagnosis of malignant disease in cases in which ordinary clinical methods fail. The chief of these newer methods is the antitryptic reaction of Brieger and Trebing, but, in addition, attempts have been made to utilise the hemolytic property of the blood serum of cancer patients, and, these proving unsuccessful, a cutaneous reaction with normal blood-cells has been introduced. During this year another, this time physical, test has been suggested—the meistagmin reaction. None of these, with the possible exception of the antitrypsin reaction, has really got past the experimental stage, but a short review of the main points brought out so far may be of interest.

Antitryptic Reaction.—Weil (Amer. Journ. Med. Sci., May 1910) gives an excellent account of the present state of knowledge concerning this reaction, which was described by Brieger and Trebing in 1908, and has since then been the subject of a large number of investigations. The claim originally made for the test—that it is exclusively characteristic of cancer—has not been upheld, for the reaction can be obtained under a variety of circumstances—after the onset of labour and in the puerperium, in Graves’s disease, on the change from breast to artificial feeding, &c. It is, however, characteristic to this extent, that it is given by nearly all cancer patients, and in only a small proportion of cases of most other diseases. The antitrypsin reaction consists in a marked increase of the power of the blood serum to inhibit the proteolytic activity of a solution of trypsin.

Methods. Two are in common use—(a) Brieger and Trebing’s method. Plates of coagulated serum are used as the medium of digestion. A constant quantity of the serum to be tested is added to increasing amounts of a standard solution of trypsin, and a loopful of each mixture is placed on the serum plate, which is then incubated for twenty-four hours at 55° C. By inspection of the plate it is then possible to determine how much trypsin can be totally inhibited. (b) Gross and Fuld’s method.
Solution of casein is used as the medium of digestion, serum and trypsin as before being added to a series of test-tubes containing equal quantities of the casein. At the end of two hours the tubes are acidified, whereupon any casein remaining undigested is precipitated. The lowest amount of trypsin which induces complete digestion indicates the limits of the antitryptic power of the serum. Weil regards the second of these as the better method, by reason of its simplicity, rapidity, absence of opportunity for bacterial action, and sharper end point. Notwithstanding alleged objections, solutions of commercial trypsin appear to be sufficiently constant for use in this test. The results are stated in figures indicative of the numbers of cubic millimetres of trypsin solution inhibited, and are comparatively, not mathematically, accurate, for Weil has shown by another ("viscosity") method that a serum which inhibits 6 c.mm. is not actually twice as active as one which inhibits only 3 c.mm. Weil finds that the two methods give results which are practically interchangeable. An increase in the antitryptic index of the blood serum occurs in 95 per cent. of all cases of cancer. All observers give quite comparable results on this point, the figures ranging from 70 to 95 per cent. Increased antitryptic power is also present in chronic wasting diseases, including diabetes and severe anaemias; in chronic infections, such as tuberculosis; in acute infections—pneumonia, typhoid, sepsis, and rheumatism; and in Graves's disease. It is therefore not characteristic of new growth, nor of cachexia. Physiologically it is met with after the transition from pregnancy to labour and the puerperium, and also in infants where artificial feeding is substituted for breast feeding.

From a diagnostic point of view a raised antitryptic index is too common to be valuable as a specific test. Its absence, however, tells strongly against cancer. If it is present in the case of a neoplasm of doubtful character, tuberculosis being excluded, is in favour of malignancy. It is so constant in Graves's disease that it may be relied on in the detection of larval forms.

From the biological standpoint, many features of the reaction are obscure. The chemical nature of antitrypsin is not known; possibly it is a lipoid, but this is doubtful. It is also uncertain whether it is a true immune body, or whether the possession of antitryptic power is merely an accidental property of the serum. Various substances—e.g. charcoal, egg albumen—act as antitryptic agents, and it has not been shown that the antitrypsin of serum is specific in its action vis-à-vis trypsin as compared with other ferments. In this respect it differs from an artificially-prepared antiferment. But although antitrypsin cannot be properly regarded as an antibody, it is reasonable to suppose that the serum containing it may have responded to a given stimulus by means of a protective mechanism (defensive against auto-digestion) which does not answer to the criteria characteristic of amboceptors and
antibodies. Theoretically, a trypsin ferment should be present in the serum, and, actually, this has been demonstrated. Such trypsin may arise from (1) pancreas; (2) polymuclear leucocytes (which contain trypsin); (3) other tissue cells; or (4) cancer cells (which contain proteolytic ferment); and arguments have been adduced in favour of each of these sources. It is suggested that in gastric canceroma the pancreas is over-active and thus trypsin passes into the blood, but this, of course, fails as an explanation of the reaction in other diseases. In acute infections it has been shown that the antitryptic reaction is related to the presence of leucocytosis, which looks as though the trypsin were set free by the destruction of numbers of these cells. In Graves's disease, typhoid, diabetes, and chronic tuberculosis, in which there is no leucocytosis, the heightened metabolism associated with cellular disintegration has been made responsible for the trypsin. In cases of cancer the trypsin originates in the tumour cells. To sum up, the origin of the hypothetical trypsin, which is supposed to act as a stimulus for the production of antitrypsin, or, technically speaking, as antigen, is as yet undetermined. It may, conceivably, arise in the pancreas, or in the leucocytes, or in the tissue cells, or in the new growth, but actual evidence that it does so arise is at the present time an absolute necessity for the establishment of the theory.

Skin Reactions in Carcinoma from the Injection of Human Red Blood Corpuscles.—Elsbey, Neuhof, and Geist publish some work in this direction in the Amer. Journ. Med. Sci. for February 1910. The fact that extracts of malignant tumours are haemolytic has led to the search for haemolysins in the blood of cancer patients, which would enable a diagnosis to be made. It has been erroneously claimed that in the early stage of cancer the blood is haemolytic, but this occurs in only about half the cases, and is also found in other diseases.

The writers conceived the idea of testing the haemolytic power of the blood by introducing washed human corpuscles under the skin of the patient. Normally, such cells would be broken up and carried away; abnormally, they might be liquefied in situ, and give rise to a local reaction. Technique.—Blood is aspirated from a vein into a syringe containing a bead which defibrinates when the syringe is shaken. A 20 per cent. suspension of the thrice-washed corpuscles is used, and may be preserved in ice for 24 to 48 hours. Five minims of the suspension are introduced under, not into, the skin of the forearm. A positive reaction begins in about 5 hours, increasing in severity, until it is at a height in about 8 hours. It may begin as early as 2 or as late as 8 hours. When the reaction is at its maximum there is an irregularly-shaped, well-defined, reddish, tender, slightly raised area, from 2 to 5 cm. in diameter, with a white areola. The colour varies from brownish-red to maroon with a bluish tinge. It fades in from 6 to 10 hours and leaves an ecchymosis. Percutaneous inoculation gave
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negative results. 684 injections were made on 432 patients, grouped as follows:—I. Cancer; II. Certainly non-cancerous; III. Probably cancerous; IV. Advanced or miliary cancer. The results are tabulated thus:—

|     | Positive | Negative | Doubtful |
|-----|----------|----------|----------|
| I.  | 62 (90%) | 5 (7%)   | 2 (3%)   |
| II. | 15 (4.6%)| 307 (94.3%) | 3 (1.1%) |
| III.| 7 (77.8%)| 2 (22.2%)| ...      |
| IV. | 11       | ...      | 11 (100%)|

Meiostagmin Reaction (μείων, small; σταγώ, a drop).—This reaction is one which is being worked out by Ascoli in the institute for special pathology of internal diseases in the University of Pavia, and as the principle involved is a new one, which may, if found trustworthy, prove of service in the study of other immunity reactions, a general résumé of the papers which have appeared (Münch. med. Wochenschr., 11th January, 22nd February, 19th April, 24th May, 31st May, 1910) may be given. The object of the test is to determine by a new method whether a given antigen reacts with a serum. In the research in question the antigens used were derived from tubercle and typhoid bacilli, as well as cancerous material. The principle underlying the test is simple. Hitherto the finer physico-chemical methods of detecting interaction between an antigen and antibody have been neglected, and it occurred to Ascoli to investigate whether, when such an interaction occurs, the surface tension of the serum is affected. The surface tension was tested in the usual way, by Traube's stalagmometer, an instrument which measures the number of drops yielded by a given quantity of fluid in passing through a fine opening. If the surface tension is high, the drops are larger and fewer; if low, the reverse. Working first with typhoid and tubercle bacilli extracts—known antigens—it was found that admixture of these with serums of typhoid and tuberculous patients increased the number of drops, thus showing that the surmise that interaction of antibody and antigen causes an alteration of the surface tension was correct. Using extracts of cancerous material as antigen, a similar lowering of the surface tension of serum from cancer patients, but not of patients suffering from other diseases, was obtained. The same phenomenon was observed with extracts of ankylostoma and echinococcus in the serums of patients suffering from ankylostomiasis and hydatid disease.