to be present by other means have we failed to obtain haemochromogen crystals.

Conclusions.

A. In the majority of cases, especially with fresh stains and if care be exercised, there is no difficulty in obtaining haemin crystals.

B. The haemochromogen crystal test, however, possesses the following advantages:

1. Simplicity of technique; being obtained in the cold by simply adding the solution (Takayama 2).
2. If it is desired to heat the slide, there is no danger of overheating as there is in the case of haemin crystals.
3. The crystals are large, easily seen, and are of a very characteristic appearance and colour.
4. The nature of the crystals may be confirmed by means of the spectroscope.

We wish to thank Professor Littlejohn for the help and advice he has given us.

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A SIMPLE TEST OF DIAGNOSTIC VALUE IN GENERAL PARESIS.

BY

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THE diagnosis of general paresis depends upon the recognition of certain mental symptoms, the eliciting of a number of physical signs, and the finding of certain definite changes in the cerebro-spinal fluid. As regards the last named, most reliance is placed on the following four points: (1) a positive Wassermann reaction, (2) a Lange colloidal gold curve of the paretic type (5555543210), (3) an increase in the amount of globulin, and (4) a pleocytosis. Two of these changes—the increase in the number of cells and in the amount of globulin—can be demonstrated with very little trouble, and hence are of the greatest value to the clinician, who is often called upon to make a quick diagnosis. Unfortunately, however, these two alone do not furnish conclusive proof of the presence of general paresis, and delay occurs until the laboratory report on the Wassermann reaction and the colloidal gold curve is at hand. The discovery, therefore, of a test which could be easily and quickly performed and which would be as reliable as the Wassermann reaction would be of considerable importance to the clinician, whether he be a consulting physician or a general practitioner.

In 1923 Boltz¹ first described a test performed on the cerebro-spinal fluid which he claimed would satisfy these conditions, and he stated, as the result of his investigations, that this test (the acetic anhydride-sulphuric acid test) was positive in every case of general paresis and was negative in all other conditions with the exception of certain cases of neuro-syphilis and an occasional case of arterio-sclerotic psychosis. In 1925 Grossman,² using the same acetic anhydride-sulphuric acid test, also found that every case of general paresis gave a positive reaction.

In the present series of cases the cerebro-spinal fluid of 180 patients, suffering from various types of mental disorder, was examined, and the result of the acetic anhydride-sulphuric acid test was compared with the Wassermann reaction, the Lange colloidal gold curve, the amount of globulin, and the number of cells.

Method of Performing the Test.

To 1 c.cm. of cerebro-spinal fluid in a small glass test tube add 0.3 c.cm. of acetic anhydride. Shake the mixture well and then carefully add, drop by drop, 0.8 c.cm. of concentrated sulphuric acid. The test tube is then held up against a white background

and the presence of a lilac tint indicates a positive reaction; a brown-yellow or red-yellow colour is noted if the reaction is a negative one. The lilac colour, characteristic of the positive reaction, may appear immediately after the addition of the sulphuric acid and disappear in a minute or so. Hence it is important to watch the cerebro-spinal fluid closely as soon as the sulphuric acid is added, or a slightly positive case may be missed. In the majority of cases the lilac tint remains for at least five minutes.

The chemistry of this test is not fully understood, but it seems probable that it depends upon the presence of cholesterol in the cerebro-spinal fluid.

Results in 180 Cases Investigated.

Of 92 cases of general paresis the cerebro-spinal fluid showed:

Wassermann reaction positive ...	...	92=100%
Acetic anhydride-sulphuric acid test positive ...	...	89= 97%
Lange curve of paretic type ...	...	84= 91%
Increased amount of globulin ...	...	90= 98%
Increased number of cells ...	...	91= 99%

Of 5 cases of neuro-syphilis (not general paralysis of the insane) the cerebro-spinal fluid showed:

Wassermann reaction positive ...	...	5=100%
Luetic Lange curve ...	...	4= 80%
Acetic anhydride-sulphuric acid test positive ...	...	2= 40%
Increased amount of globulin ...	...	4= 80%
Increased number of cells ...	...	5=100%

Of 83 cases of other types of mental disorder the cerebro-spinal fluid showed:

Wassermann reaction positive ...	...	0=0%
Acetic anhydride-sulphuric acid test positive ...	...	1=1%
Lange curve of positive type ...	...	1=1%
Increased amount of globulin ...	...	5=6%
Increased number of cells ...	...	1=1%

Consideration of the above results shows that the acetic anhydride-sulphuric acid test gives a positive reaction in practically every case of general paresis (97 per cent.). Of the three exceptions one was an undoubted case of general paresis with the typical mental symptoms, well marked physical signs, and positive cerebro-spinal fluid findings. The other two cases, however, were by no means typical, and were probably very early cases in which there were few mental changes, some physical signs, and a slightly positive Wassermann reaction in the cerebro-spinal fluid. In another case, a well marked general paretic, the Wassermann reaction of the cerebro-spinal fluid and the Lange curve were found to be negative on the first examination, but the acetic anhydride-sulphuric acid test was strongly positive and the amount of globulin and the number of cells were slightly increased. A second specimen of the fluid was examined a fortnight later, and this time a very faintly positive Wassermann reaction (+3) was obtained, the cells and globulin were slightly increased, the Lange test was negative, and the acetic anhydride-sulphuric acid test was again strongly positive. In this case, therefore, the acetic anhydride-sulphuric acid test was more sensitive than the Wassermann reaction. The degree of positivity of the acetic anhydride-sulphuric acid test in cases of general paresis does not vary directly with that of the Wassermann reaction. Thus certain cases with a faintly positive Wassermann reaction in the cerebro-spinal fluid gave a strongly positive result with the acetic anhydride-sulphuric acid test and vice versa. In a number of instances the cerebro-spinal fluid was obtained from general paralytics who had undergone a course of malarial treatment. In these it was found that although the Wassermann reaction had in most cases become less strongly positive the acetic anhydride-sulphuric acid test showed no change. Compared with the Lange reaction in general paretics the acetic anhydride-sulphuric acid test would appear to be more sensitive and more reliable, since a positive result with it was obtained in 97 per cent. of these cases, as against 90 per cent. in the case of the Lange test. In cases of neuro-syphilis (not general paralysis of the insane) the Wassermann reaction was positive in all, the acetic anhydride-sulphuric acid test only in 40 per cent. In the 83 other cases which were investigated (cases of epilepsy, manic-depressive psychosis, senile dementia, dementia praecox, alcoholic and arterio-sclerotic psychoses, etc.) only one case, a patient suffering from senile dementia, gave a faintly positive reaction with the acetic anhydride-sulphuric acid test.

Summary.

As a result of these investigations it would seem justifiable to draw the following conclusions:

1. The acetic anhydride-sulphuric acid test on the cerebro-spinal fluid of cases of general paresis is positive in almost every case (97 per cent.), and hence is almost as reliable as the Wassermann reaction in this condition.
2. It is negative in almost every other type of mental disorder except certain cases of neuro-syphilis (other than general paralysis of the insane).
3. It is a test which can be performed with great ease and rapidity and hence is of definite value to the clinician.

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ON THE SOMATIC ORIGIN OF MALIGNANT DISEASE.

BY

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THE view of malignant disease here presented is simple, congruous, as it seems to me, with ordinary pathology and ordinary clinical medicine, reconciles easily and naturally the discordant and puzzling results of recent experiment, and, if true, removes most of the obscurity and mystery from the malignant process.

Malignancy and Hyperplastic Inflammation.

Clinicians have long held the opinion that continued irritation will induce cancer. This opinion has been confirmed by exact observation on the effect of various irritants, especially the extracts of tar; by these, as is well known, the disease has been brought on in mice by direct experiment. Now the chief reaction of the body to a chronic irritant is a proliferation of connective tissue and epithelium. This process is commonly called chronic inflammation; it is well seen in the chronic mastitis which so often precedes carcinoma of the breast. Sir Lenthal Cheate objects to the term "inflammation" as a description of this process; it differs, indeed, in degree and partly in kind from acute inflammation, but resembles it in being a reaction to mild, as the other to intense, irritation; and, like the acute kind, seems to be essentially a vascular and lymphatic reaction, though in acute inflammation the vascular changes prevail, and in chronic inflammation the lymphatic.

Sir Lenthal Cheate's accurate and careful observations¹ seem to show that this process of hyperplasia may pass almost imperceptibly into an innocent or malignant tumour. He has shown specimens where in a single breast chronic mastitis has developed into fibro-adenoma and different varieties of carcinoma. Dr. Archibald Leitch's experiments on guinea-pigs² lead to the same conclusion. He was able to produce malignant growth in the gall bladder of the guinea-pig, a refractory animal, by means of gall stones, or even sterile pebbles, aseptically introduced. He, too, is quite sure that there is no clear dividing line between carcinoma and simple hyperplasia. "We have," he says, "no means of determining when the heterotopy and irregular growth of the tubular epithelium ceases to be translatable as simple hyperplasia and assumes the definite characters of malignant neoplasia . . . the process is so gradual and the dividing line so imperceptible."

Malignancy not a Property of the Tumour but a Reaction of the Body.

It seems most improbable, as Dr. Leitch remarks, that any toxic agent should have arrived from elsewhere to change so utterly the nature of the growth yet change its habit and appearance hardly at all; nor could any such

agent have been introduced under the conditions of the experiments, nor probably have been present originally in the gall bladder. I would suggest that the malignant alteration is most simply explained if we suppose that the tumour, or hyperplasia of epithelium, does in fact remain unchanged; that the change from innocency to malignancy consists wholly in an altered reaction of the body. At some moment, we will say, the body becomes aware of this mass of cells, regards it as a living intruder, and attacks it with leucocytes and cytolytics. If the epithelial cells are finally surrounded by fibrous tissue the tumour is "innocent"; it is thenceforth disregarded as a foreign body. But if this encirclement fails, the growth is "malignant"; the malignancy, however, is not in the tumour. There is a fatal difference between this and an invading microbe; the tumour is not foreign to the body, but part of it; the cytolytics which are lethal to the tumour cells are lethal also to the cells of the body. Hence the zone of destruction at the periphery of a malignant growth, the corrosion of muscles and blood vessels and nerves; hence also the fretting of the tumour's surface, the metastases, and general cachexia; all this destruction is wrought, if my view is true, not by the juices of the tumour, but by the juices of the body. It is probable that a vicious circle begins, that the tumour cells which are not destroyed are irritated to more rapid growth, and the body thus stimulated to fiercer efforts; however this may be, the whole malignant process seems in this manner quite easily explained.

Practical Tests.

From acceptance of this view it would follow that if the body could be induced to ignore the tumour the whole malignant process would stop; but how to achieve this is not easy to see; the patient might be hypnotized, but hypnotic suggestion must be carried far to induce a leucocyte to slacken its activity; it seems unlikely that this method would succeed. Again, we might inject some chemical body like a vaccine, but of opposite effect, so that the activity of the body against a specific invader would be not stimulated but depressed. Such a chemical body may be invented in the future by bacteriologists. If the body in the part affected could be made anaesthetic by blocking its afferent nerves it seems possible, but not certain, according to this view, that the malignant process would be arrested or retarded. The reactions of inflammation are probably in large measure the result of chemiotaxis, and so would proceed though sensation were destroyed; still, the tumour would be unfelt and vaso-dilatation abolished. The feeble resistance offered by ataxic patients to perforating ulcer of the foot would seem to afford some hope that the malignant process might thus be checked.

I had arrived at this point when I learnt that this experiment had already been tried—deliberately on mice by Dr. Cramer, and by Nature on sundry patients whose cases are recorded by Sir Lenthal Cheate. Dr. Cramer³ painted a number of mice with an extract of tar, both on the normal skin and on a part deprived of its nervous connexions. Twelve of these mice developed malignant tumours, and it is noteworthy that in every single case the normal skin was so affected. In five mice malignant growth arose also in the denervated area, but so late, in three of these, that it seems almost certain that the nerves of the part had regenerated themselves before growth began. Thus, in all but two of the mice malignant growth was inhibited by the loss of nerves; moreover, in one of these two exceptions the growth of the tumour was slow and malignancy but slight.

It must be admitted that these experiments do not go very far toward the proof of the case. It may be said that if, as seems likely, malignant disease is a reaction of the body cells to irritation, then that reaction might probably fail if the irritation could not be perceived. Nevertheless, with the old view of cancer, malignant proliferation might seem a reaction of cell protoplasm to a local stimulus rather than a reaction of the body as a whole to an irritant; once allow this, and we are fairly launched on the road to my conclusions. Now, Cramer's experiments, though not conclusive, do strongly suggest that malignant disease is a reaction of the body as a whole,