THE SERUM DIAGNOSIS OF PREGNANCY AND OF CANCER:

A CRITICAL STUDY OF ABDERHALDEN'S METHOD.

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I. THE THEORY OF PROTECTIVE FERMENTS AND ITS PRACTICAL APPLICATION TO THE SERUM DIAGNOSIS OF PREGNANCY.

AN amazingly fruitful period in the progress of our knowledge of pathological processes was ushered in with the discovery that the blood serum in certain germ-caused diseases possessed the property of destroying these organisms or of neutralizing their toxic powers. There resulted from this, inspired, helped, or hindered by the theories of conflicting schools, countless experiments that taught us to recognize the fact that the blood serum gives evidence of reaction bodies (immune bodies) to very diverse substances (antigens) that have gained access to the system. Diverse though these substances be at first sight, they can all be classified as complicated proteins. They may be bacteria, toxins, products of vegetable origin, tissues or tissue constituents of other animal species, but they are all foreign to the economy of the particular animal into which they have been introduced by the breaking down of some natural barrier of defence. It is almost certain that the activities of all the reaction bodies towards such foreign substances are differently manifested in test-tube experiments and within the body, but by means of these test-tube experiments we can form some idea of the defensive mechanisms.

When we come to deal with substances less foreign to the body, such as the cells or cellular proteins of other animals belonging to the same species, the biological methods hitherto employed are generally useless to detect the presence of any reaction substances in the serum. That the system elaborates means of defence against them is evident, but we almost always fail to find evidences of that defence in the serum. It is true that occasionally such evidence may be forthcoming, but it is haphazard at the best. For example, Ehrlich, on one occasion, by injecting into a goat overwhelming amounts of the lysed corpuscles of other goats, produced in the serum a reaction body capable of setting free the haemoglobin of certain goats' corpuscles, but the experiment has never been successfully repeated, and had it not been that the name of this great authority was attached to the observation the possibility of its occurrence would have been disputed. At the most it is a rare experimental phenomenon, and no general conclusion can be drawn from it—a point that must be borne in mind when considering the details of Abderhalden's theory. Sometimes human serum exhibits a certain amount of haemolytic power towards the corpuscles of other individuals, and attempts have been made to connect this phenomenon with certain diseased states, but it is very inconstant, and is without any diagnostic value. Experiments in tissue transplantation, and especially the numerous experiments in mouse cancer inoculation, have shown us that the resistance to such grafts is very feeble, and, though an artificial resistance may be induced, it, too, is feeble and transitory, and no evidence of it is traceable in the blood serum by any present methods.

Few and fortuitous as these results are with substances so closely allied as the tissues of other animals of the same species, they are absolutely negative when we attempt to trace reactions to injections of an animal's own tissues. A resistance of a kind to mouse cancer inoculation may be induced by the previous injection of mouse spleen, but the injection of the animal's own splenic tissue is followed by no resistance whatever. This experiment, which we owe to Woglom, is one of the most important in recent cancer research, and quite crushed the expectations entertained by enthusiasts of being able to induce a specific resistance to cancer along the lines of previous research. Four years ago I endeavoured by injections of their own corpuscles into rabbits, subcutaneously or intramuscularly, every other day for a period of six weeks, to produce a haemolytic reaction body in the serum, but the experiments were quite negative. We have, in short, no experimental evidence along

the lines on which we have gone that the blood serum shows any power of dealing with the cells of the body by producing reaction substances to them. We cannot, however, deny the possibility of the metabolic products of injected cells being dealt with by some bodies that may be present in the serum. Let me take an example that will focus the problems. In cancer we have a progressive growth, beyond their natural confines, of cells that have sprung from the normal body cells and still retain many of the parent properties. Apart from the extremely rare instances of spontaneous cure, the body shows no resistance against these cells; no state of immunity is induced. They go on growing, and they finally produce death. Omitting those cases in which the cancer prevents the discharge of some vital function, why should the disease be fatal? It can only be that these cells set free metabolic products which, either by their nature or by their amount, upset the regulating mechanisms of the body. It may quite well be that though there is no lethal reaction-body elaborated against them yet an attempt is made to cope with their products. And the question is, how is this attempt made? Are these products dealt with by the normal body cells, or does the blood serum acquire the power of breaking them up into less harmful constituents? If the latter could be shown to be the case we might hope to trace the changes. Here the genius of Abderhalden illumined the beginnings of a road into the fruitful unknown.

Abderhalden imagines that just as the cells of the intestinal tract have at their disposal ferments which split up the complicated food constituents into simple products suitable for absorption, so the cells of the body, having taken what they require from the blood, build it up and break it down into suitable combinations by the help of ferments. Thus in normal circumstances. But if anything foreign gains access to the blood stream, without having undergone preliminary degradation in the alimentary canal, then new and specific ferments are elaborated capable of breaking it down into simple constituents. These new ferments, originating without doubt in the body cells, will be set free in the blood plasma, and as we can only detect a ferment by means of its specific activity, so their presence will be demonstrated if we trace what occurs when the ferment-containing serum is brought into contact with the foreign substance on which it acts, or to use the appropriate nomenclature, when the specific *substrate* is provided. If we add gastric juice to such a protein as egg-albumen we find that the latter is digested into peptones in virtue of the presence of the ferment pepsin. Similarly we test for the presence of proteolytic, peptolytic, or inverting ferments in the blood by adding the plasma or serum to proteins, peptones, or sugar and observing the changes produced in these substrates. We cannot recognize a ferment apart from its action. This being so, it is obvious that we are faced with the question, Given the changes we should expect from the action of a ferment, are these changes due to the ferment or are they due to other causes? We shall only be entitled to assume ferment action when we can rule out of account the operation of all other factors producing the same result. This is the crux of Abderhalden's theory, and, as I shall show later on, he has not taken into account the extent of the other factors that contribute to the results on which he depends.

Abderhalden depends on two chief experiments for the basis of his theory. In the first place, he claimed to have observed in the blood plasma or serum of animals which had been injected with foreign peptone (that is, a peptone not derived from their own tissues) a ferment action on these peptones. This experiment was made by taking a mixture of the serum of the treated animals and a solution of the peptone, observing the polarimetric reading at once and noting the change produced after the lapse of varying periods of time. With the fresh serum of untreated animals or with the heated serum of treated animals (the heating would of course destroy the fermentative power) the initial rotation did not alter, whereas with the unheated serum of treated animals it increased. This observation he verified by repeated experiments. The second set of experiments dealt with the changes produced in mixtures of sugar solutions and the serum of animals which had previously had parenteral injections of sugar. In both cases the polarimetric readings were taken

to demonstrate the presence of peptolytic or inverting ferments respectively. In neither case, if one may take as typical the graphic representations which he gives, was the rotation considerable. The extreme rotation is to be reckoned not in degrees, not even as a rule in tenths of a degree, but in hundredths of a degree; and even supposing we were to admit that such small rotations were conclusive evidence of cleavage of the substrate by a ferment, yet even with the most delicate polarimeters and with the most experienced eyes it is gravely to be doubted if any one working with such a complicated substance as serum can be certain of reading with such meticulous exactitude. We know serum to be very unstable, and very slight departures from the strict isotonicity of added fluids are capable of producing evident changes in it. Generally speaking, it is questionable if polarimetric readings are more delicate than titration methods, and in such an important fundamental experiment it is unfortunate that Abderhalden neglected to bring forward the confirmatory evidence that could be supplied by such methods. He states, however, that the polarimetric readings in the experiments with protein are confirmed by the dialysation method, which will be considered in detail afterwards, and he admits that in the sugar injection experiments the desired results could only sometimes be obtained. If the serum of rabbits which have received injections of egg-albumen be added to this egg-albumen and the mixture dialysed, it will be found that the amount of ninhydrin-reacting substances in the dialysate is not appreciably, if at all, increased beyond the amount obtained when normal rabbit serum is used. I have repeated in rabbits his sugar experiments, but have failed to convince myself that any increase of the initial polarimetric rotation was produced or that the amounts of glucose found by titration differed when the mixtures of sugar and unheated serum were compared with those of sugar and heated serum. Complement deviation experiments were quite negative. In view of the experiments of Weinland previous to those of Abderhalden, and of those of Röhman and Kumagai subsequently, there is some independent support for this part of his claim, but there is considerable divergence as to how the result may be produced and as to what actually occurs.

But however favourably we view these fundamental experiments, we cannot fail to notice that the reactions claimed are against substances, quite foreign to the animal, which have gained access to the circulation in an abnormal way. And just as we have seen in discussing the reactions of immunity that there were reaction-bodies elaborated against proteins quite foreign to the animal body, scarcely any at all when the proteins were foreign to the animal but proper to the species, and none whatever when the proteins were derived from the animal itself, so it behoves us to be cautious before accepting a sweeping theory in which similar experimental links are wanting, all the more so because Abderhalden recently has brought his protective ferments into line with the immune bodies. That this is no captious criticism is evident from some experimental work published by Pincussohn and Petow.¹ These observers found that the normal serum of an animal has the power of splitting up the muscle peptone of its own species or that of allied species, but manifests no such action against the muscle peptone of foreign species. Indeed, the average polarimetric rotation in these experiments was greater than the small rotation depended on by Abderhalden for the diagnosis of pregnancy. If this observation be correct, then the polarimetric readings which have been relied on in the diagnosis of pregnancy and diseased conditions must be received with great suspicion. Human serum will break down placental peptone, not because the serum is that of a pregnant woman and the peptone is derived from a placenta but just because the serum and the peptone are from human beings.

In pregnancy there is a new organ interposed in the economy, existing only for a time. It will take up from the blood certain constituents for its requirements and it will return to the circulation certain products of metabolism, and it is assumed that these are dealt with, not so much by endocellular ferments as by special specific ferments in the plasma elaborated *ad hoc*. It seems rational, but it may or may not be true. Whether the placenta sets free into the blood characteristic proteins which are broken up

by the supposed proteolytic ferments is a question vaguely discussed, but it seems to be assumed that the ultimate cleavage products of a protein are capable of calling forth a whole order of ferments acting specifically on all the higher combinations of these constituents. Thus, for example, the introduction of a peptone into the blood may call forth in response a ferment for the protein from which the original peptone was derived as well as a ferment for the peptone itself.

Two separate methods are employed for the detection of the presence of ferments, the polarimetric method by which the degradation of peptones may be observed, and the dialysation method by which the degradation products of proteins may be separated. The latter is the method on which most of the work has been done. According to Abderhalden, the results of the two methods always agree. I have used the dialysation method solely in the following experiments. If we take the procedure adopted in the diagnosis of pregnancy as an example, the technique is briefly as follows:

Fresh healthy placental tissue from which the blood clot has been removed is cut up into pieces and washed until it is colourless. It is boiled several times in five times its volume of distilled water, until the water when filtered fails to give a colour when boiled with 1 c.cm. of a 10 per cent. solution of ninhydrin. The pieces of placental tissue may then be stored in sterile distilled water under a thick covering of toluol. These pieces contain the coagulated placental protein, in addition, of course, to other substances which are not of immediate importance, and they serve as *substrate* for the demonstration of the ferment action. The serum under examination for the presence or absence of specific ferments is obtained by removing a quantity of blood from the patient by venipuncture, and allowing this to clot spontaneously. Special dialysation tubes are used, which are supposed to retain proteins and to allow peptones and amino-acids to diffuse through. These tubes are placed in 20 c.cm. of sterile distilled water in small Erlenmeyer flasks. Into one tube we put a teased-out portion of the placental tissue (roughly about $\frac{1}{2}$ to 1 gram) and add to this a certain fixed quantity of the serum (either 1 c.cm. or 1.5 c.cm.), taking care to avoid any of the serum getting into the water outside the tube. Into another tube, which is to serve as a control to this test, we put 1.5 c.cm. of the serum only. In both cases we cover the contents of the tube and the surrounding water in the container with a thick layer of toluol in order to prevent evaporation and bacterial contamination. The tubes are incubated at 37° C. for sixteen hours. At the end of that time 10 c.cm. of each dialysate is removed and tested with 0.2 c.cm. of ninhydrin solution, the test tubes being boiled uniformly for exactly one minute. A violet colour denotes the presence of peptones or amino-acids.

Supposing a specific proteolytic ferment is present in the serum, then the dialysate of the first tube will contain peptones and amino-acids, and these will be demonstrated by the violet colour with ninhydrin. If the ferment is absent, then there will be no production of peptones and no reacting substance will be found in the dialysate. On the other hand, the dialysate of the second tube, containing serum alone, will show no ninhydrin-reacting substance, because there is no *substrate* on which the ferment can act; the water will remain colourless. However, some serums contain diffusible substances in sufficient amounts to be detected in the dialysates by ninhydrin, and in such cases we shall have to judge of the presence or absence of specific ferments by the comparative depths of colour in the two tubes. If, therefore, we obtain a violet colour when we add ninhydrin to the dialysate of a tube containing serum *plus* placenta, and no colour (or one much less marked) with the dialysate from the tube containing serum alone, then the conclusion is that the individual from whom the serum was taken is pregnant. If no colour is found in the case of either tube, or no comparative difference of colour, then the individual is not pregnant. Similarly for the diagnosis of certain diseased conditions: in cancer we employ cancerous tissue as substrate; in exophthalmic goitre, thyroid tissue; and so on.

The method has a wide application in the serum diagnosis of disease. Hundreds of papers have been published giving uniformly good results. The conception has deeply stirred the minds of investigators in all parts of the world. It is true that there have been a few doubters, but these sceptics are met with the constant assertion that their methods are faulty, and that they have not taken into account certain possible fallacies.

These fallacies can be invoked to explain away almost every conceivable mistake in diagnosis.

We must seriously ask ourselves if the method is to be relied on for information in clinically doubtful cases. According to Abderhalden, the proper reading of the result is never wrong—a claim that reminds one of the Delphic oracle.

The method of performing the reaction, which has been sketched roughly above, is given in very voluminous detail in Abderhalden's *Abwehrfermente des tierischen Organismus* and in numerous publications in various journals. The method is by no means difficult, and the technique is easy to follow. A method that cannot be carried out by the average laboratory worker who exhibits ordinary care is not of much utility. Though I have worked with this reaction for more than eighteen months, I have rejected the results obtained during the first half of that period, so as to avoid the criticism of being unfamiliar with the technique. During that first period, however, the results were much more favourable to Abderhalden's claims than afterwards. The reason is not far to seek. Captivated by the theory which opened up for us great possibilities in cancer investigation, carried along by the host of communications that hailed the method as well-nigh infallible, perhaps intimidated by the scorn poured on the few that doubted, I accepted uncritically the good results, shut my eyes to those that were doubtful, and found excuses to reject those that were adverse—for a time. In the later period, when I was untrammelled by authority, it was found that the results were far from supporting the claims put forward. The technique given by Abderhalden was slavishly followed. His retort to that is: "I treat such assertions with the scepticism born of a rich experience." Such a reply might be overwhelming if his own published technique were above reproach. I can only say that I have done my best to follow his directions without actually having made the customary pilgrimage to Halle to receive the direct apostolic revelations from the master.

In the following examples of the practical application of the method I first investigated the reaction in pregnancy because the true diagnosis of the condition cannot long remain in doubt and we are soon enabled to verify our results. It is seldom that the condition is doubtful, and the serum diagnosis of pregnancy would only have a limited value. In cancer, on the other hand, a method of serum diagnosis would be of the utmost practical importance. I have tried all the methods hitherto advocated; they are all worthless in practice. But if the procedure of Abderhalden was capable of giving good results in pregnancy it might reasonably be expected to give good results in cancer, though the relation of the placenta to the maternal organism is not strictly comparable to the relations existing between malignant tumour cells and the rest of the body. In every case here recorded the true diagnosis is known. To prevent the knowledge of the condition of the patient furnishing the serum having any effect on our reading of the reactions—a vital point—the tubes were numbered, the numbers written down for later identification, and the tests conducted and the final readings made without being aware of the clinical diagnosis of the conditions. It is impossible to avoid bias otherwise. Again, the tests were manifolded. It sometimes happened that very strange results were recorded. For example, the controls might give deeper colours than the actual tests themselves, or the readings might be equivocal throughout any set. In such cases I rejected the result altogether as well as the dialysation tubes in these cases. The colours obtained with ninhydrin varied from light lilac to deep violet. In making a comparison between the tubes I have neglected weak tints, representing these as negative, except where there was a difference between the test and its control, and in this way I have been generous towards the method. The deepest colours are represented throughout by +++.

The figures in Table I show that 34 cases gave more or less clear positive results, but two cases were absolutely negative; in these two cases the serum was quite fresh. In one of these cases the clinical diagnosis was doubtful; the reaction was negative; the further history of the case showed that the patient was three months pregnant at the time. Positive reactions are therefore the rule in cases of pregnancy, and have been found much more frequently in this than in any other condition I have examined. Unless I have been unconsciously generous in my readings to the

TABLE I.—Tests with the Serum of Pregnant Cases.

Thirty-six cases were investigated. For most of the material I am indebted to my friend Dr. S. J. Cameron, of Glasgow (26 cases). These serums were sent to me by post and were two to four days old when used. In the other 10 cases I withdrew the blood myself, six of these patients having been sent to me by my colleague Mr. Dinnick.

	Age of Pregnancy, etc.	Serum alone 1 c.cm.	Serum alone 1.5 c.cm.	Placenta, + 1 c.cm. Serum.	Placenta, + 1.5 c.cm. Serum.
1	Second month	0	0	0	0
2	" " " " " "	0	0	+++	+++
3	Second month (pelvic abscess)	0	0	++	+++
4	Second month (pernicious vomiting)	—	0	—	+++
5	Third month	0	0	+	+
6	" " " " " "	0	0	0	0
7	Third month (aborting) ...	0	0	+++	+++
8	" " " " " "	0	0	++	+++
9	Fifth month	0	0	++	+++
10	Fifth month (albuminuria)	—	0	—	+++
11	Sixth month	0	+	++	+++
12	Sixth month (pernicious vomiting)	0	0	+++	+++
13	Seventh month	0	0	+++	+++
14	" " " " " "	0	0	0	++
15	" " " " " "	0	0	++	+++
16	Eighth month	0	0	++	+++
17	" " " " " "	0	0	++	+++
18	" " " " " "	0	0	+++	+++
19	Ninth month	0	0	+++	+++
20	Ninth month (threatened eclampsia)	0	0	+	+
21	Full term	0	0	0	++
22	" " " " " "	—	0	—	+++
23	" " " " " "	0	+	++	+++
24	" " " " " "	0	0	++	++
25	" " " " " "	0	0	+++	+++
26	" " " " " "	0	0	+	++
27	" " " " " "	0	+	+++	+++
28	Full term (syphilitic) ...	—	++	—	+++
29	" (eclampsia) ...	—	0	—	++
30	" (eclampsia) ...	—	0	—	+
31	Three hours after delivery	0	0	++	++
32	Twelve hours after delivery	0	0	+++	+++
33	Twenty-four hours after delivery	—	0	—	+++
34	Ectopic gestation (fifth week)	0	0	+++	+++
35	Ectopic gestation (second month)	0	0	+++	+++
36	Ectopic gestation (tenth week)	0	0	+++	+++

The serum in Nos. 4, 10, 12, 15, 17, 27, 28, 32, 34, was haemoglobin tinted; in the other cases it was free. In Nos. 1, 34, 35, 36, more than four hours elapsed between the taking of a meal and the withdrawal of the blood; in the other cases I am unaware of the times elapsing.

theory, or unless the serum of pregnancy is more unstable than is the rule in other conditions, then a certain amount of support might be accorded to Abderhalden's idea of specific guardian-ferments.

Control Tests with the Serum of Other Gynaecological Conditions.

Particulars of the eleven cases tested are given in Table II. The first case of chorion-epithelioma was only detected after hysterectomy had been performed. There was no suspicion of its presence, but the reaction, as we might have expected, was positive. The serum was again examined after an interval of twenty days, and again one month later, no symptoms or signs of metastases having manifested themselves, but the reaction in both cases was still positive. The case of endometritis (No. 4) might possibly have been one of retained products of conception, as the curettings were not microscopically examined. The other three cases that gave clear positive results

were not pregnant (two of them being re-examined with the same result), and are practical demonstrations of the unreliability of the reaction. No. 6 was considered clinically to be a pregnancy of the third month; the reaction was positive; the case was followed up; she was not pregnant, and had not aborted. The last case of uterine fibroid (No. 11) is of interest because there was a conflict of opinion as to its nature, and the Abderhalden reaction was twice invoked to assist in the diagnosis. Twice it pointed to pregnancy; the surgeon removed the uterus; it was a soft fibro-myoma, and there was no pregnancy. The times that elapsed between meals and the withdrawal of the serum in this case are unknown to me.

TABLE II.—Control Tests: Gynaecological Patients.

	Disease.	Serum alone, 1 c.cm.	Serum alone, 1.5 c.cm.	Placenta + 1 c.cm. Serum.	Placenta, +1.5 c.cm. Serum.
1	Chorion-epithelioma ...	0	+	++	++
2	Uterine polypus ...	0	0	0	0
3	Vaginismus ...	0	0	0	0
4	Endometritis ...	0	0	++	++
5	Uterine fibroid ...	—	0	—	0
6	Dysmenorrhoea ...	0	0	++	++
7	Pyosalpinx ...	0	0	++	++
8	Uterine fibroid ...	0	0	0	0
9	Uterine fibroid ...	0	0	0	0
10	Chorion-epithelioma ...	0	0	+++	+++
11	Uterine fibroid ...	0	0	+++	+++

All the serums were fresh. Only the serum of No. 5 was haemoglobin-stained. The blood in all cases, with the exception of No. 11, was withdrawn at time of operation.

Control Tests with the Serum of Cancer Patients.

The following cases were all operable, and the blood was withdrawn from them at the time of operation when they were in a fasting condition.

TABLE III.—Control Tests: Cancer Patients.

The first 10 cases are females, the other 12 males. In Nos. 7 and 17 only had the serum a haemoglobin tint. Throughout the tests were duplicated, with the same results as given below.

	Disease.	Serum alone, 1 c.cm.	Serum alone, 1.5 c.cm.	Placenta, + 1 c.cm. Serum.	Placenta, +1.5 c.cm. Serum.
1	Carcinoma of breast ...	0	0	0	0
2	" " ...	0	0	0	+
3	" " ...	0	0	+	++
4	" " ...	0	0	+	+
5	" " ...	0	0	0	+
6	Carcinoma of breast (recurrent)	+	+	+	+
7	Epithelioma of tongue ...	0	0	0	+
8	Carcinoma of splenic flexure	0	0	+	+
9	Carcinoma of rectum ...	0	0	+	++
10	" " ...	0	0	0	0
11	Epithelioma of lip (early)	0	0	++	++
12	Epithelioma of tongue ...	0	0	+	+++
13	" " ...	0	0	0	++
14	Epithelioma of tonsil ...	0	0	0	+
15	Epithelioma of fauces ...	0	0	0	0
16	Epithelioma of larynx ...	0	0	+	++
17	Epithelioma of penis ...	0	0	0	0
18	Epithelioma of bladder ...	0	0	0	0
19	Carcinoma of rectum ...	0	0	0	0
20	" " ...	0	0	0	+
21	" " ...	0	0	++	++
22	" " ...	0	0	+	++

In No. 6 dialysis of the serum against running water for a few hours failed to remove from the serum all its dialysable ninhydrin-reacting constituents. I have frequently noticed this, and it is pro-

bably due to the progressive spontaneous cleavage of the serum proteins. I cannot vouch for the sterility of a serum after it has undergone dialysis against running water, but I do not think that bacterial contamination has much to do with the result.

Several authors have said that cancer serum may break down placental protein, whilst others deny this. If both in pregnancy and in cancer there exist ferments in the serum capable of degrading placental and cancer-cell protein respectively, we should expect *a priori* that these ferments would operate on allied substrates, though perhaps to a lesser extent, because none of the immune reaction bodies that we know is strictly specific. Abderhalden recommends that only placenta should be used in the pregnancy reaction which fail to give reactions with cancer serums. Personally I have never encountered such a placenta, and I doubt if it exists.

Control Tests with Serums from Normal and other Conditions.

With the exception of Nos. 1, 2, 9, 18, 21, 24, 25, 26, in which the length of time that elapsed between the last meal and the withdrawal of the blood is unknown to me, all the others were operation cases, and the blood was removed at the time of operation.

TABLE IV.—Control Tests: Normal and other Conditions.
Cases 1 to 20 are females; 21 to 31 males.

	Condition.	Serum alone, 1 c.cm.	Serum alone, 1.5 c.cm.	Placenta, + 1 c.cm. Serum.	Placenta, +1.5 c.cm. Serum.
1	Normal female ...	0	0	+	+
2	" " ...	0	0	0	0
3	Chronic appendicitis ...	0	0	++	++
4	" " ...	0	0	0	+
5	Cholecystitis ...	0	0	0	0
6	" " ...	0	+	0	+
7	Cholecystitis (impacted stone)	0	+	+	+
8	Tuberculous adenitis ...	0	0	0	0
9	Lupus ...	0	0	0	0
10	Lipoma of arm ...	0	0	0	+
11	Lipoma of shoulder ...	0	0	0	+
12	Adenoma of breast ...	0	+	0	++
13	Pyloric stenosis ...	0	0	0	0
14	" " ...	0	0	0	0
15	Intestinal adhesions ...	+	+	+	+
16	Inguinal hernia ...	0	0	0	0
17	Hydrocele of hernial sac...	0	+	+	+
18	Tertiary syphilis ...	0	0	0	0
19	Proptosis of sigmoid colon	0	0	0	0
20	Abnormality of caecum ...	0	+	0	+
21	Normal male ...	0	0	+	+
22	Wound of lip ...	0	0	0	0
23	Tuberculosis of lip ...	0	0	0	0
24	Syphilitic glossitis ...	0	0	0	0
25	Locomotor ataxy ...	0	0	0	0
26	Tertiary syphilis ...	0	0	0	0
27	Pyloric stenosis ...	0	0	0	0
28	" " ...	0	+	0	+
29	Tuberculous peritonitis ...	0	+	+	+
30	Haemorrhoids ...	0	0	+	++
31	Chronic appendicitis ...	0	0	+	++

The serum of Nos. 13, 19, 23, 24, 25 was haemoglobin-stained; in No. 25 the serum was more deeply stained than in any other case examined. All the serums were fresh.

This table shows, better perhaps than any of the others, that different readings can be obtained as we compare the tubes containing 1 c.cm. of serum, or those containing 1.5 c.cm. of serum; but taking the readings of the two sets together and leaving out of account the indications

given by a single set, we find that the best we can say for the reaction is that it makes mistakes in 5 cases out of 31. If we believe firmly in the reaction, we may make excuses for two of these five cases (1 and 21) by saying that the blood was withdrawn too soon after a meal, and we may excuse the other three palpable lapses by saying that we must have committed some error of technique, for no man is infallible, and we can the more readily accord the vice of fallibility to others than to ourselves. Judging from the large amount of other work that Abderhalden turns out of his laboratory, it is scarcely possible that he can have personally attended to the examination of the very large number of cases on which he or his assistants have reported.

Summary.

To sum up the results of the above 100 cases tested to prove the diagnostic worth of the dialysation reaction in pregnancy, we find that by the most generous reading possible, judging by two sets of experiments and not by the usual one, making allowances for all the hypothetical fallacies, we have still 17 most glaring mistakes in diagnosis, which of itself is a large percentage, sufficient to destroy the diagnostic worth of the reaction. But if we apply to the good results the same code of ethics by which we reject the undesired, then the whole theory becomes worthless.

In a second article the question of protective ferments in cancer will be considered, and the inherent fallacies of the method will be examined in detail.

REFERENCE.

¹ *Biochem. Zeitsch.*, October 23rd, 1913.

Presidential Addresses

TO THE

BRANCHES OF THE BRITISH MEDICAL ASSOCIATION.

BORDER COUNTIES BRANCH.

NATIONAL HEALTH INSURANCE.

BY

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IN the first place permit me to express to you my best thanks for the honour you have done me in electing me President of the Border Counties Branch. It is a position I appreciate very highly. Our Association has been and is passing through troublous times. We have had dissensions within and attacks from without; a rush to join our ranks when danger threatened; withdrawals and resignations when these same persons failed to get all their own way. Grumbings we have had in plenty, because the Association failed to secure all the advantages for the profession that these most exacting critics demanded—the critics being for the most part those who did nothing themselves either for the Association or the profession, but thought apparently that membership of the Association entitled them to be spoon-fed with benefits without any effort on their own part.

These tribulations, however, we have survived, and will survive; they should only serve to bind more closely together those who have the best interests of the profession and the Association at heart. For the interests of the profession and the interests of the Association are one, and the Association is doing its best work when it is safeguarding the interests of the profession at large and not of any particular section.

The National Health Insurance Act directly affects the great majority of the profession, and profoundly alters their relation to their patients, to the general public, and to the State. Even those who are not on the panel are bound to be affected sooner or later, for it is quite certain that this Act is only the beginning of still greater changes. Dependants will be brought within its scope; institutional treatment cannot for long be confined to tuberculosis; our general hospitals cannot be expected to undertake the wholesale treatment of insured persons and continue to

be supported by voluntary contributions. State aid or municipal aid will have to be accorded them, and this inevitably involves more or less State or municipal supervision. The Act has already checked the flow of voluntary contributions. It will doubtless continue to do so in an ever-increasing degree. Where the end will be no one can tell.

Certain it is, however, that greater changes than we have yet seen will be brought about, and it behoves us to consider and anticipate these changes, so that, as far as possible, they may be so controlled and directed as to secure the best possible results for the profession and the public weal.

I believe most strongly that there is no subject of such vital importance to the profession at the present time, and none so essential to the welfare of our patients, as the establishment on a sound and just basis of the relation that is to exist in future between doctor and patient. That the old relation is to be changed fundamentally none can doubt. It has been altered already for some fifteen million persons, and a vast majority of the profession. The full extent of the change is not yet appreciated, but it is not the less on that account a change of the most radical kind, and whether it is to be for better or worse depends very largely on the wisdom of the course taken by the profession as a whole, and the unity and singleness of purpose with which they persist in carrying out what they conceive to be the best policy alike for themselves and for their patients.

We have to recognize the fact that insurance is the law of the land, and that the vast majority of the medical profession have accepted service under the National Insurance Act as it is. What I want to insist upon to-day, with all the force of which I am capable, is that we are not on that account to consider that there is nothing more for the profession to do than merely go on quietly and submissively attending to the bodily ailments of our patients, leaving the arrangements for organization and control of the relations between the doctors and their patients to committees and Commissioners. It is now for the first time that the necessity has arisen for doctors to attend to their own business. Under the conditions of State insurance unless the doctors look after their own interests they will certainly suffer. The State undertakes that the insured person shall have proper medical attention, and the insured person himself expects it, and the approved societies complain that the demands on their funds are excessive. Amongst so many contending forces the doctor will fare badly unless he can protect his own interests, and this he is absolutely unable to do individually against such powerful influences. Let no one suppose that finality has been reached in the arrangements made for providing and paying for medical attendance, or in the conditions imposed upon doctors.

The National Insurance Act, 1911, only came into operation, so far as medical service is concerned, in January, 1913, yet an amending Act was passed during 1913, and only pressure of other business in Parliament has prevented the introduction of another amending Act in 1914.

We know that the approved societies are exerting their influence to secure that the next amending Act shall restore to the societies the "control of their own doctor," as they term it. We know one great reason for this to be that many of the societies have been very hard hit. The amount of sickness benefit they have been called upon to pay has greatly exceeded their estimate, and they desire the control of the doctor because they think it will enable them to influence him in the direction of giving fewer certificates of incapacity for work, and such as he does give for shorter periods.

I think myself that both the societies and the doctors made a mistake in the first instance in attaching too much importance to this matter of control of the doctor, to the neglect of other and more important issues. When the Insurance Bill was first under discussion it was generally anticipated that the "approved societies" contemplated in the bill were the old-established friendly societies, such as the Oddfellows, Foresters, and the like, together with clubs providing medical attendance as one of their benefits in connexion with certain localities or industries. The inclusion of trade unions, and more especially of the large industrial insurance associations, amongst the approved societies has entirely altered the outlook. I think the objection on the part of doctors to