which there was almost complete deafness before the operation, and that for a considerable period. In 12 cases the voice can now be heard at least 18 feet off, and in 11 cases over 12 feet off; that is, in 23 cases (46 per cent.) the hearing power remains or has been restored to a degree sufficient for most practical purposes.

On comparing the operation of ossiculectomy with the complete mastoid operation, the following points may be mentioned.

In favour of ossiculectomy.—1. The large number of cases which can be cured or in which the mastoid operation may be avoided. 2. The large proportion in which a good result is obtained with regard to the hearing power. 3. The slight inconvenience of the operation to the patient and the short duration of the after-treatment.

Against ossiculectomy.—It has been urged that in many cases the mastoid operation eventually may become necessary, even although an apparent cure or cessation of discharge may be obtained for a short period after ossiculectomy has been performed, and also that the minor operation does not render the patient completely free from further risk of intracranial complications. With this I do not agree, and I hope the cases I have quoted will support my contention.

It is no doubt true that the above objections to ossiculectomy may have held good some years ago, when the operation was not performed so thoroughly and the outer attic wall was not removed. It must also be admitted that in a certain number of cases, owing to the formation of adhesions, the hearing power, although very good soon after the operation, may eventually become worse. But this, however, may also take place after the complete mastoid operation.

Speaking generally with regard to middle-ear suppuration, I feel sure that if Schwartz's operation (simple opening of the antrum and mastoid cells) were performed more frequently in those cases in which the discharge did not cease within two months, the suppurative process might be arrested and the hearing power in many cases might be restored to normal. But if, on the other hand, the surgeon only sees the patient after the suppurative process has existed for a lengthy period, then I consider that if conservative treatment fails, ossiculectomy, if possible, should be given a trial before performing the complete mastoid operation, unless this is absolutely imperative.

Harley-street, W.

ISO-HÆMOLYSIS IN RELATION TO CANCER.¹

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Iso-hæmolysis in Malignant Disease.

FROM time to time clinicians and pathologists have sought for some sign of malignant disease which should lend greater accuracy to the diagnosis of this condition. This hope would seem at first sight to be futile when we consider the different morphological types of malignant disease and the various situations in which it may occur. Yet on further observation it is seen that malignant tumours have certain points in common, and the most characteristic of these is their tendency to unlimited peripheral growth, while the cells in the middle and older parts of the tumour perish from lack of nutriment.

The surgical treatment of cancer is based on the assumption that it is, in its inception, a local condition; but the later stages of its growth are associated with general emaciation and anæmia—the cancerous cachexia—which would seem to indicate that some product of the cancer enters the circulation and exerts a harmful effect on the general metabolism. Whether this toxic substance arises from the autolysis of the malignant cells or is a secretion of the proliferating part of the tumour it is evident that it must be sought in the blood, and it is the blood cells and serum in malignant disease that have attracted most attention.

The existence of hæmolytic substances in the serum of certain individuals has been known for many years, but there has recently been a renewal of interest in the subject, stimulated chiefly by the work of Weil of New York and Crile of Cleveland.

In the course of his work on the infective lymphosarcoma of dogs Weil found that extracts of these tumours possessed the power of laking the red corpuscles of normal dogs. This was more particularly the case when the tumours had undergone central necrosis. He further discovered that the blood serum of dogs affected with this condition, especially when the tumours were breaking down, acquired hæmolytic properties. Following this Weil tested human sera in a series of 82 cases, 31 of which were malignant. He divides his results into four groups: (1) Serum which does not hæmolyse its own but hæmolyses alien cells; (2) serum which hæmolyses its own and alien corpuscles; (3) serum which hæmolyses its own but not alien corpuscles; and (4) serum which does not hæmolyse its own or alien corpuscles.

—	Group 1.	Group 2.	Group 3.	Group 4.
Early malignant tumours...	6	2	1	6
Late malignant tumours ...	9	2	2	3
Benign tumours	1	0	1	1
Other diseases... ..	11	0	2	29
Normal	0	0	0	6

He concludes that the results in human beings are less characteristic than in the case of the dog tumours, and this is only to be expected since the dog tumours are all of one morphological type.

Crile's work attracted considerable attention by reason of the large number of cases examined and the remarkably high percentage of positive results he obtained in cases of cancer. He also described a "reverse reaction" frequently noted in cases of tuberculosis, a disease which, like cancer, is often associated with a hæmolytic serum. This "reverse" reaction is said to be present when the patient's red cells are laked by normal serum. Crile found that the serum was hæmolytic in 85 per cent. of the cases of cancer, and, contrary to Weil's observation, noted that it was more marked in the early cases. The high diagnostic value given to this test by Crile has led to the publication of the results obtained by numerous other workers, the greater number of them giving a far lower proportion of positive reactions in cancer.

Janeway studied 35 cases of cancer. Seven were early cases, or cases with a small amount of malignant tissue present; 4 of these were positive. It is noteworthy that all four were recurrent growths. There were 18 late cases, of which 7 were positive. There were also 10 examples of cancer of the face, of the rodent-ulcer type, only 1 of which was positive; this was an advanced case. The total percentage of positive reactions was 48.5. He met with one positive reaction in a case of chronic mastitis.

Ottenberg and Epstein examined 100 cases. These were taken in groups of 10 or 15, the serum of each one being tried on the cells of every other member of that group. Of the 100 subjects 38 were malignant, 40 had other diseases, and 22 were apparently healthy. Of the cancer cases 28 had hæmolytic serum (76 per cent.), and 20 of the cases with other diseases were positive (50 per cent.); 6 of these were tuberculous, 5 being hæmolytic. Among the other diseases which gave positive results were 3 benign tumours, 2 fibroadenomata of the breast, and 1 diffuse lipoma. One of the 22 normal cases showed hæmolysis. A strong hæmolytic reaction was present in 50 per cent. of the cancer cases, and in only 17 per cent. of the 40 other cases. If the resistance of the corpuscles was considered as well as the reaction of the serum, it was found that a hæmolytic serum generally laked non-cancer cells, but did not affect cells from a cancer patient, or was lytic to both kinds of cells according as it was weakly or strongly hæmolytic. If attention was paid only to the resistance of the red cells it was seen that red blood cells resistant to all sera occurred chiefly in those cases whose serum was itself hæmolytic, and not much more frequently in cancer than in other diseases. On the other hand, resistant red cells were obtained rarely from cases with non-hæmolytic serum. These authors are inclined to agree with Weil in associating the hæmolytic property of the serum with the autolytic products of necrosis, though it is noteworthy that the sera of four early tumour cases were strongly hæmolytic.

Smithies examined 85 cases affected with various ailments. Twelve of these were cases of cancer, of which 7 (58.3 per cent.) were hæmolytic, 3 negative, and 2 undetermined.

¹ A paper read before the Leeds and West Riding Medico-Chirurgical Society.

There were 2 benign tumours, both negative; and 15 cases of tuberculosis, 1 positive, 6 negative, 6 undetermined, and 2 reverse. Of 12 cases of syphilis, 1 was positive, 8 were negative, and 3 undetermined. Of 25 other non-malignant affections, 5 were positive, 13 negative, 6 undetermined, and 1 reverse. He describes a positive reaction as one in which the cancer serum destroys normal cells, while the cancer cells are not destroyed by normal and frequently by cancer serum. If hæmolysis occurs in both the reaction is called undetermined. In the malignant cases those more advanced gave the most marked reactions. Generally speaking, the reactions were more marked in the malignant than in the other cases.

The results obtained by Johnstone and Canning approach more nearly those of Crile. Of 43 cases of carcinoma 37 were positive (80·6 per cent.). Nine cases of sarcoma gave 100 per cent. positive results, though the reactions were not as marked as in the carcinoma cases. Two endotheliomata were positive; 14 benign tumours were all negative. Of 43 cases of tuberculosis 7 gave reversed reactions, the remainder were negative. The sera of 103 persons suffering from other diseases gave 17 positive reactions. There were 4 positive reactions among 85 normal individuals; these 4 cases were all negative when re-examined in a day or two. In all the malignant cases re-examined the reaction was constant. There were not many cases of superficial epitheliomata among this series.

Butler examined 22 cases of cancer, mostly of the stomach, uterus, and breast. The sera of 13 of these (59 per cent.) were hæmolytic, some hæmolysing the corpuscles of other cancer patients. Three out of 8 tuberculous sera were hæmolytic; reverse hæmolysis was not seen. In 2 cases of cancer the serum was hæmolytic for the corpuscles of the same individual (auto-hæmolysis).

Richartz obtained a positive reaction in 46 per cent. of 74 malignant cases; those most advanced were generally negative.

The results obtained by Whittemore differ remarkably from the foregoing. He tested the sera from 101 persons. Thirty-nine of these were normal among whom 7 had hæmolytic sera. Among the remainder were 22 cancer cases, none of whom had hæmolytic sera, but the corpuscles from 8 of these patients were hæmolysed by normal sera. This reverse reaction was seen in 4 out of 8 tuberculous cases and in 4 out of 32 patients suffering from other diseases. The only 2 hæmolytic sera shown in his table belong to this group, one a case of sarcoma of the antrum and the other a general paralytic.

Blumgarten, following Weil's technique, has tested the serums of 75 patients, 25 of whom were suffering from advanced cancer. Eighteen of these (72 per cent.) hæmolysed normal corpuscles, while only 1 per cent. of the normals and cases of other diseases were hæmolytic.

An interesting comparative study of the hetero-hæmolytic and iso-hæmolytic properties of cancerous blood has been recently published by Kelling, who has had a most extensive experience in this work. He gives a table of 100 cases in which the blood was tested against human and fowl's corpuscles. On the showing of the table there appears to be an advantage, from the diagnostic point of view, in favour of heterolysis, but he thinks that if the intensity of the reaction is taken into consideration the facts are otherwise and that the method of iso-hæmolysis possesses fewer sources of error.

Technique.

After carrying out a few observations by Crile's method it seemed desirable to evolve a technique which would not necessitate the abstraction of so large a quantity of blood, and after various trials I adopted the following method as requiring a minimal quantity of serum.

A small quantity of blood is obtained from the finger and collected in two glass capsules in the ordinary way. One of the capsules is sealed and set aside to allow of clotting. To the other sample is added an equal quantity of citrated saline (0·85 per cent. sodium chloride, 0·85 per cent. sodium citrate in distilled water); the tube is shaken and put aside until the test is to be set up. After a few hours the clot is extracted from the first tube and the serum centrifuged until free from corpuscles. The corpuscles in the other tube are separated by centrifuging and washed with saline (0·85 per cent.) three times. All the samples of normal and diseased blood collected at approximately the same time are treated in a similar way.

A length of quarter-inch glass tubing is drawn out in the flame at intervals of two inches and is then divided up into a number of capsules. Each capsule is filed across at its middle and the narrow ends sealed, thus forming a series of miniature test tubes or goblets.

Each goblet is filled from a pipette with a few drops of pure liquid paraffin which is then shaken or centrifuged down to remove air bubbles. The capsules are then stuck upright in a Petri dish filled with plasticine and numbered.

With a capillary pipette, freshly rinsed in saline, a minute drop of serum is allowed to fall into each goblet where it will sink slowly through the oil and come to rest just above the narrow part. The number of tubes needed will depend on the sera to be tested. Serum from a suspicious case should be tried on all the available corpuscles. Each normal serum should be tried on the corpuscles of all other normals. Each pair of goblets receives the same serum, the right hand goblet of each pair being the control. The controls are then placed in order in a water bath and kept at a temperature of 55° to 60° C. for ten minutes to destroy the complement. After being inactivated the controls are returned to their place in the dish, which is placed in cold water until all the tubes have reached the same temperature.

Each pair of goblets then receives a drop of the appropriate corpuscles in 20 per cent. emulsion. By using an emulsion of this strength instead of 5 per cent., as is customary, it is possible to use only a minute drop and thus avoid diluting the mixture.

The tubes are kept in the incubator at a temperature of 37° C. for two hours and the results then read off.

It is usually recommended that the tubes should be kept in the cold for 12 hours after incubating before noting the results, but this is unnecessary when dealing with such small quantities, for the corpuscles sink to the bottom in two hours. Nothing is to be gained by cooling the mixture before incubation, and there is no advantage in keeping the tubes in the incubator longer than two hours.

Hæmolysis in the unheated tube but not in the heated control is recorded as a positive result; if hæmolysis occurs in both tubes it is to be regarded as due to an error in technique, and the observation is to be repeated; but with care in using clean tubes and pipettes I have only rarely found this necessary. All results should be read within 24 hours of the abstraction of the blood.

Results.

The sera of 86 individuals have been examined.² These may be divided into five groups.

Group 1.—Carcinoma, 34 cases. 17 of these were hæmolytic, 15 were negative, and 2 doubtful. Eliminating these two cases there are 56·25 of the carcinomatous sera which gave positive results. In 18 cases the resistance of the corpuscles was tested; the cells were resistant in 9, one of which had a non-hæmolytic serum; and in the remaining 9 the cells were non-resistant. One of these came from a blood whose serum was hæmolytic. If these cases are grouped according to the locality of the growth it is evident that the proportion of cancers with hæmolytic sera varies with the seat of the disease.

—	—	Hæmolytic.	Non-hæmolytic.	Doubtful.
5	Lip and tongue.	1	3	1
1	Maxilla.	0	1	—
7	Esophagus.	3	3	1
1	Stomach.	1	0	—
4	Colon and rectum.	4	0	—
10	Breast.	7	3	—
5	Uterus (cervix).	0	5	—
1	Vulva.	1	0	—
34	—	17	15	2

If the cases are viewed in the light of the histological type of growth it is seen that the spheroidal and columnar-celled carcinomata furnish the majority of the hæmolytic sera.

All cases were diagnosed by microscopic examination or by the naked-eye appearances at operation except five cases

² For the opportunity of observing many of these cases I am indebted to the courtesy of my colleagues on the infirmary staff.

of cancer of œsophagus, in which the diagnosis rested on clinical evidence, two cases of cancer of the breast, one a typical early scirrhus (positive), and a late ulcerating cancer, and one advanced inoperable epithelioma of lip.

Group 2.—Sarcoma, 5 cases. One of these was hæmolytic, the remaining 4 were negative. The hæmolytic serum was from a case of sarcoma of the humerus, while the negative sera came from cases of sarcoma of the tonsil, hand, sternum, and kidney.

Group 3.—Tuberculosis, 8 cases. 4 of these cases were positive, 3 were negative, and 1 was doubtful. In addition to these there were 2 negative cases in which the clinical evidence of tubercle was very questionable.

Group 4.—Other affections, 27 cases (including cases of rheumatoid arthritis, syphilis, malaria, hyperthyroidism and hypothyroidism, gastric ulcer, chlorosis, chronic bronchitis, and subacute and acute pancreatitis). 22 of these were negative, 3 were doubtful, and 2 gave positive results. Of these two hæmolytic sera, one was from a youth with a chronic hydrocele; no sign of tuberculous disease of the testis was noted at the operation. The other was from a man with paroxysmal hæmoglobinuria. This serum was interesting in that it was not only hæmolytic for the corpuscles of two normal individuals, but it also dissolved the red cells from two persons with hæmolytic sera (cancer of the breast and tuberculous osteomyelitis) which were each resistant to the other's serum. Furthermore, the hæmoglobinuric serum did not hæmolyse when mixed with corpuscles and placed in the incubator at once, but hæmolysis occurred if the mixture of red cells and serum was cooled for half an hour before incubation, in this respect differing from the other hæmolytic sera examined. This serum was not autohæmolytic; it was drawn in an interval between attacks. Four of the negative cases in this group were benign tumours (two myomata, a papilloma of the bladder, and a papilloma of the larynx), and one a peritoneal endothelioma.

Group 5.—Normals, 10. All negative. One of these was a negro.

Relation of Iso-hæmolysis to Iso-agglutination.

That there is some relation between these two phenomena is suggested by the fact that a lytic serum will agglutinate those corpuscles against which it is hæmolytic. In only a few instances have I directed special attention to this point, but these have shown the above to be true. Dudgeon states that iso-agglutination occurred whenever iso-hæmolysis was demonstrated. On the other hand, iso-agglutination is of common occurrence in many diseases, whereas iso-hæmolysis is less frequent. The hæmo-agglutinins are, like the hæmolytic immune bodies, thermostable, but they do not need the presence of complement for their action, whereas the hæmolytic immune body does not dissolve red corpuscles in the absence of thermolabile complement. Thus a hæmolytic serum inactivated by heat will produce agglutination without hæmolysis. And further, as became evident in the saturation experiments to be described, the red cells are susceptible to agglutinins in the cold just as they are capable of absorbing hæmolytic amboceptor at a low temperature. In spite of these resemblances between iso-agglutinins and hæmolytic amboceptors Dudgeon concludes that the agglutinative and hæmolyzing properties of normal or immune sera on red blood cells have no direct relation to one another.

Resistance of Red Cells.

The red cells from a blood whose serum is hæmolytic are generally capable of resisting the action of a hæmolytic serum from another individual. Among 24 samples of hæmolytic bloods the resistance of the corpuscles was tested against another hæmolytic serum in 11, only one of which was laked. Nine of these 11 were from malignant disease. In no case did I find corpuscles destroyed by the serum of the same individual (auto-hæmolysis). If the reactions in the test-tube are at all comparable with the changes occurring *in vivo* it would be reasonable to expect the red cells to acquire a resistance to their own hæmolytic serum, for otherwise hæmoglobinuria would not be an uncommon event in cancer even through a chill, as claimed by Eason, were necessary to enable the cells to absorb the amboceptor. As for the phenomenon of reverse hæmolysis in tuberculosis I have not seen it. On the contrary, the behaviour of the red cells from a tuberculous hæmolytic blood appears identical with that of the cells from a case of malignant disease. It should be noted here that this reverse

hæmolysis was observed by Dudgeon in cases of typhoid, syphilis, and pneumonia, and in some cases not only were the immune cells laked by normal serum but the immune serum of the same patient hæmolysed normal corpuscles. I have already alluded to the results obtained by Whittemore; his tables show that 16 out of 18 examples of hæmolysis were produced by the action of normal sera on immune red cells. This is in keeping with the fact that 7 of his 39 normals were hæmolytic.

The resistant quality of the red cells appears to depend on their inability to absorb amboceptor. This is shown by the following experiment. Cooled hæmolytic serum from a case of carcinoma of the colon was placed in two tubes—A and B. Tube A was saturated with my washed corpuscles; tube B with washed corpuscles from a case of cancer of the breast (whose serum was hæmolytic). Both tubes were kept in the cold for half an hour and then centrifugalised, the resulting sera, A1 and B1, being pipetted off, and the sedimented corpuscles, A2 and B2, being washed three times in saline. My fresh washed corpuscles were added to tubes A1 and B1, while my fresh serum was added to tubes A2 and B2. After two hours' incubation hæmolysis had taken place in tubes A2 and B1, but not in A1 or B2.

As suggested above the cells from a hæmolytic tuberculous blood seem equally incapable of absorbing the malignant hæmolytic amboceptor as illustrated by the following experiment, which also serves to bring out another point—namely, that the blood from some cases of malignant disease, though itself showing no appreciable hæmolysis, may yet furnish red cells which are resistant to other hæmolytic sera. Inactivated hæmolytic serum from a cancer of the breast was placed in three tubes—A, B, and C. Tube A saturated with my washed cells; tube B with cells from a boy with phthisis; and tube C with cells from a cancer of the œsophagus (whose serum was not hæmolytic). After cooling for half an hour the tubes were centrifugalised into serum and corpuscles, the former being placed in tubes A1, B1, and C1; the latter, after washing, into tubes A2, B2, and C2. Tubes A1, B1, and C1 were reactivated with fresh normal serum and to each was added washed normal corpuscles. Fresh normal serum was added to tubes A2, B2, and C2, and they were all incubated two hours. Hæmolysis occurred in tubes A2, B1, and C1, but not in A1, B2, or C2.

Deterioration of Hæmolytic Sera.

If a hæmolytic serum be kept sealed up in glass capsules it is found to lose its power of laking normal corpuscles in a few days (within a week), but its power may be restored by the addition of fresh normal serum, though not if the fresh normal serum has been inactivated by heat. This loss of activity is therefore due to absence of complement which is altered by keeping just as it is by exposure to a temperature of 55° C., that is to say, the complement is not destroyed but is changed in such a way that though it has lost its power of producing hæmolysis it is capable of acting on a mixture of amboceptor and red cells at body temperature and so preventing hæmolysis on the subsequent addition of fresh complement. The following is the experiment. Ten-day old hæmolytic serum was saturated with normal corpuscles in two tubes, A and B. A was placed in the incubator for half an hour; B was kept in the cold for the same length of time. They were then centrifugalised and the sera pipetted into tubes A1 and B1, the corpuscles being washed and placed in tubes A2 and B2. Fresh normal serum and washed normal corpuscles were added to tubes A1 and B1, and fresh normal serum to tubes A2 and B2. After half an hour's incubation hæmolysis had occurred in B2, but not in the other three tubes.

I have found the hæmolytic amboceptor to be active one month after being drawn; it is thus possible to keep a supply of a known hæmolytic serum at hand which, when reactivated, may be used for testing the resistance of red corpuscles.

The Hæmolytic Test in Vivo.

A year ago Elsberg conceived the possibility of a cutaneous hæmolytic test. His idea was that if normal corpuscles were injected beneath the skin of a patient with hæmolytic serum they would be laked and might produce a visible discolouration of the skin. In a recent paper embodying the results of a number of tests carried out on these lines he states that 77.5 per cent. of 80 cases of carcinoma (or 90 per cent. excluding the very advanced cases) gave a positive skin reaction, while 94 per cent. of the negative reactions

were in patients free from carcinoma. I have, so far, only tried this test in six patients, all with negative results. Three of these had sera which, *in vitro*, hæmolysed the corpuscles injected.

Conclusions.

It is evident that the possession of iso-hæmolysins is very far from being pathognomonic of cancer. But then very few signs of the disease in its curable stages will bear this interpretation. A reaction which is positive in 50 per cent. of patients with cancer deserves, I think, to be weighed in the balance with other facts in the endeavour to arrive at a diagnosis. The only other conditions likely to be confounded with cancer in which hæmolysis is frequently met with are tuberculosis and pernicious anæmia, especially the former. In such cases, if hæmolysis be proved, it is possible that one of the forms of tuberculin reaction would be of value. A negative hæmolytic reaction can, of course, carry no weight.

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Hull.

FURTHER OBSERVATIONS UPON TYPHOID CARRIERS.¹

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SINCE the publication of the last report² we have investigated several methods of treatment and have made daily examinations³ of the excreta of another typhoid carrier for a period of 15 months. The results obtained appear to justify the prolonged study of one particular case, and to suggest that some of the conclusions and recommendations of those who claim successful eradication of the typhoid bacillus from the human tissues by means of this or that method of treatment would be modified or withdrawn were the carriers subjected to more rigorous and continued examinations.

These daily examinations made such great demands upon our time that we were compelled to limit the methods employed. Consequently, we were unable to make any experiments upon the bactericidal, or opsonic, properties of the blood serum and had to confine our observations to the enumeration of the typhoid organisms in fæces and urine, to the agglutinin contents of the serum, and to the action of therapeutic agents.

¹ D. S. Davies is responsible for the public health aspect of the case, J. Fletcher for the clinical observations and collection of material, and I. Walker Hall and E. Emrys-Roberts for the bacteriological examinations.

² THE LANCET, Nov. 28th, 1908, p. 1585.

³ There were several occasions when the daily sample did not reach us owing to some difficulty in transport, but for practical purposes the phrase is, perhaps, permissible. The exact dates are given in a separate report to the health committee of the Bristol corporation.

The Action of Lactic Acid Bacilli upon *B. typhosus* and *B. coli*.

Prior to the discovery of our further typhoid carrier, one of us (I. W. H.) examined some 15 strains of lactic acid bacilli, and a number of yeasts, in order to determine the inhibiting action of these organisms upon the typhoid and coli strains isolated from the carriers previously reported upon. A summary of the results shows that while varying degrees of inhibition of coli growth were obtained, the inhibitory effect upon the typhoid bacilli was very slight—practically *nil*. This finding is in accord with the experience of some who have given the soured milk therapy a prolonged trial. It suggests that in those reported cases in which the typhoid bacilli disappeared from the excreta after a course of this treatment, the typhoid organisms were of an attenuated type, or that the disappearance of the typhoid bacilli from the excretions was a natural event rather than an effect of the therapy. It lies near to hand, also, to think that the latent bacillary period may have exceeded the period of examination in these cases. As yet the data for defining these periods are too few.

The Present Carrier Case.

X. Y., a female, aged 33 years, had typhoid fever in July, 1905. In 1905, September, her sister had an attack of typhoid fever.
 „ „ December, her brother and father had typhoid fever.
 „ 1907, July, another sister had typhoid fever.
 „ „ X. Y. took a situation as cook. In July of the same year the parlour-maid and housemaid were attacked by the same disease.
 „ 1908, September, her kitchenmaid had typhoid fever.
 „ „ December, a nurse who was looking after the carrier patient developed typhoid fever. (X. Y. had been admitted voluntarily into the Bristol General Hospital under Professor J. Michell Clarke.)

While in the Bristol General Hospital in 1908 typhoid bacilli were identified and isolated from her urine, and upon two occasions from her fæces, while her blood serum gave good agglutination reactions. She was later transferred to the Bristol Ham Green Fever Hospital for further observations. The organisms disappeared from the urine on April 13th, 1909, and the agglutinative power of the blood serum fell gradually during 1909. Although daily examinations of the fæces have been made throughout no further excretion of typhoid bacilli has occurred, and it is probable that the two early findings were due to contamination of the fæces by urine. The carrier has therefore been classed as one of the urinary type.

No typhoid organisms appeared in the urine during the remainder of 1909, but on Jan. 4th, 1910, typhoid bacilli appeared in the urine and the agglutinating power of the blood commenced to rise. The organisms continued to be excreted until Feb. 27th, 1910. Since then, although the urine has contained many coliform and other organisms, typhoid bacilli have been absent.

Clinical course.—On admission to the Bristol General Hospital on Nov. 28th, 1908, under Professor Michell Clarke, the general condition of the carrier was fair, the only symptom complained of being an occasional throbbing in the abdomen. She was somewhat thin, but the thoracic and abdominal organs were healthy. A trace of albumin was present in the urine. On removal to Ham Green Hospital on Jan. 26th, 1909, under Dr. D. S. Davies and Dr. J. Fletcher, she continued in fair health and gradually gained in weight. The slight albuminuria persisted. At the commencement of 1910, when typhoid bacilli reappeared in the urine—the patient was not made aware of the fact—she complained of slight malaise, a “crampy” feeling in the lower part of the abdomen, and pain across the small of the back. There were also occasional headache and vomiting. About the middle of March the symptoms disappeared. From January to March she lost weight but regained the loss during April. Throughout there has been neither bladder pain nor pain during micturition, nor increased frequency.

Temperature.—This has been subnormal in type, varying from 97° (morning) to 98° F. (evening). When the vaccine injections reached a dose of 1000 millions there was a slight rise to 98°–98.5°, persisting for 14 days. On Jan. 9th, 1910, about a week after the typhoid bacilli appeared in the urine, the temperature gradually rose to 99.4° and fell within 14 days to its usual level. Since then it has remained about 97.5°–98.5°.

Collection of material and methods.—These details call for mention here only because of the difficulties of inhibiting bacterial growth in human excreta. Ham Green Hospital is situated some distance from our laboratories and we were