but to the mechanical changing of the patient's environment. The specific gravity of the water is 1020, and the body is supported very lightly on the buttocks, the shoulders, and the back of the head, with the toes just touching the end of the bath to prevent the legs from floating free. The bath itself shares the rolling and pitching of the ship, but the water it contains has not time to respond, and keeps its level, with the patient immersed in it partaking of its relative immobility. Watching a bathful of water in a rolling ship the surface appears to slant this way and that with the movement of the vessel, but a spirit level floated on a cork raft will show that the water is unaffected. If the ship is pitching the long axis of the bath should be fore and aft; if rolling, athwart ship. The patient must not be able to see the apparent oscillation of the water, and the eyes should be bandaged—voluntary shutting is not enough, since in many cases vertigo is increased by the effort of closing the eyelids. If this procedure is carefully followed it always, in my experience, lessens the dizziness and gives relief, which is valuable in severe cases, and often permanent.

FATAL SUPPRESSION OF URINE CAUSED BY LATENT HAEMAGGLUTININS.

BY

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FOLLOWING blood transfusion with an apparently compatible donor, the occurrence of a condition akin to blackwater fever, both in its symptoms and morbid anatomy, and sometimes with a fatal issue, is fortunately uncommon. Blaker and Dodds (1925)¹ record with illuminating detail two such fatal cases, and add very valuable experimental observations. Keynes² refers to a case reported by Bernheim³ where, after transfusion, haemoglobinuria occurred, and progressively increased until the function of the kidney became so much interfered with by deposits of haemoglobin or damaged corpuscles that the patient died with suppression of urine and all the signs of uraemia. Dyke⁴ mentions two cases of haemoglobinuria due to a Group 2 case being mistaken for a Group 4 owing to a low titre, Group 3 serum being used for the preliminary testing. Keynes² also refers to non-fatal transient haemoglobinuria, and I myself have noted this phenomenon on two occasions.

It is of interest in this connexion to note that Yorke and Nauss,⁵ working on the pathology of blackwater fever, injected rabbits with haemoglobin and produced intrarenal obstruction. Blaker and Dodds, repeating these experiments, found that in order to produce renal precipitation the urine must be acid and contain sodium chloride to the strength of at least 1 per cent.

Comparing three fatal cases, one of mine and two of Blaker and Dodds,¹ all have certain clinical features in common: onset within a few hours; pyrexia 99° to 104°; jaundice; methaemoglobinuria; and lumbar pain with symptoms of uraemia. One case was fatal in four days, my case in eight days, and the third in nineteen days. Nitrogen retention was apparent, and the cases took on the picture of latent uraemia.

One of the Blaker and Dodds cases showed a blood urea of 102 mg. per cent. on the fourth day, 178 mg. on the tenth day, 400 mg. on the sixteenth day, 618 mg. on the seventeenth day, and 803 mg. per cent. after death. The second showed a blood urea of 287 mg. per cent., and my case on the third day showed 174.6 mg. per cent.

Clinical History of the Present Case.

A woman, aged 36, was admitted to the Princess Alice Memorial Hospital, under Mr. A. H. Crook, with a history of five and a half weeks' amenorrhoea, except for a slight "loss" four days before admission. She had a black discharge, with abdominal pain, constipation, and vomiting. She was very blanched and restless, and had the obvious appearance of severe haemorrhage of some

duration. She was very tender and rigid in the left iliac fossa, and there was dullness in the flanks, with a fluid thrill. Her pulse was 140, the respirations 28, and the temperature 97.5°.

During the operation a pint of the husband's blood was transfused after preliminary cross-testing of the patient's serum against the donor's cells for thirty minutes at room temperature and with the aid of the microscope. Both donor and patient were identified as Group 4 (Moss). At the operation the abdomen was opened by a median incision and much dark blood and clots oozed out, also a small foetus. The right Fallopian tube was found to be ruptured; it was tied and removed. The clots and blood were swabbed out and the abdomen was closed. The wound remained clean subsequently, and the patient showed very slight signs of reaction, the temperature rising only to 100.8°.

After-History.

On the next day (June 20th, 1927) the general condition of the patient was very good; she talked cheerfully, but slight icterus was noted, and there was complete suppression of urine. She complained of some abdominal pain, which was probably renal. A catheter was passed and 6 oz. of blood-stained urine were obtained, full of blood debris. The pulse was 116, the respirations 24, and the maximum temperature 99.5°.

June 21st. Suppression was complete. A catheter yielded only 2 oz. of blood-stained urine. The maximum temperature was 99.5°, the pulse 100, and the respirations 24.

June 22nd. Only 1½ oz. of urine were obtained by catheter. Hot-air baths, rectal salines, pilocarpine, and alkalis were given without effect. The blood urea was found to be 174.6 mg. per cent. The pulse was 100, the respirations 24, the temperature 99.2°, and the van den Bergh reaction was an indirect positive.

June 23rd. Only 2½ oz. of urine were removed by catheter. Lumbar pain was now marked. The pulse was 92, the respirations 22, and the temperature 98.6°.

June 24th. Only 1 oz. of urine obtained. Abdominal distension was noted, and diuretin was given without effect. The pulse was 88, the respirations 20, and the temperature 98.4°.

June 25th. Signs of uraemia appeared in addition to haemolytic jaundice, and the patient became drowsy and irritable. The systolic blood pressure was 119 and the diastolic 78. The temperature was subnormal.

The patient died suddenly on June 27th.

Post-mortem Examination.

The necropsy was performed in my absence by the house-surgeon, Dr. J. F. Lang. Early adhesions were evident between the wound and the site of removal of the ruptured ectopic gestation. The kidneys were enlarged and of a pale coffee colour, with engorgement showing as striations in the medullary rays. The capsule stripped readily. The cortex was diminished in width; it contained some engorged vessels as striated lines, but the most striking feature was the marked engorgement of the medullary rays. Microscopical sections revealed intense engorgement of the capillaries and tubules. Bowman's capsules gave evidence of compression, and the tubular cells showed flattening and pressure atrophy with disappearance of many of the nuclei. The tubules were full of red blood cells or debris, and there was cloudy swelling where the condition was furthest advanced. The development of fine, intertubular connecting tissue was visible. The kidney was clearly the seat of advanced parenchymatous changes due to lack of nutrition of the cells, which was in turn due to pressure atrophy and toxic changes. Eosin-staining material in masses and granules was evident in parts. The bladder contained coffee-ground material. In regard to the liver, the bile ducts were markedly outlined macroscopically, and the picture of chronic venous congestion was present (nutmeg type). Microscopically there were similar changes due to intense venous congestion with consequent pressure atrophy of the cells leading to parenchymatous degeneration, as evidenced by cell vacuolation and loss of nuclear staining. The spleen was very congested. Other organs were macroscopically normal.

The cause of death was therefore presumably uraemia due to mechanical blockage of the kidneys and liver by blood cell agglutination proceeding slowly and progressively owing to the presence of small but effective amounts of agglutinin in the patient's serum. Undetected incompatibility was obviously the cause. The patient and donor were apparently both Group 4, but a subsequent repetition of the cross-test (donor's cells and patient's serum) revealed at the end of sixty-five minutes a definite macroscopic agglutination. It will be remembered that thirty minutes had been allowed, and in the desperate condition of the case no longer delay was permissible. In the paper by Blaker and Dodds¹ it is recorded, in connexion with their first fatal case, that there had been some question as to the group interpretation, and, in regard to the second, both donor and recipient were apparently Group 4, but subsequently a cross-test showed the patient's serum to agglutinate the donor's cells. On more than one occasion I have found that an apparently Group 4 donor's cells were agglutinated by a patient's serum (apparently also Group 4). A similar effect was recently noted by Dr. Dyson of St. Mary's Hospital.

Dyke⁴ has noted that Group 3 serums are sometimes deficient in agglutinins, whereas others are of high titre. Professor Freuchen of Copenhagen informs me that, in a series of 400 transfusions, he has met the same phenomenon on four occasions, and the solution of the difficulty is the *invariable marketing of high titre Group 3 stock serums*—an observation recommended to commercial firms for attention.

Meanwhile, we have the cross-test. Dyke⁴ quotes the technique of the American Society of Immunologists, which considers that thirty minutes at room temperature is sufficient prevention of untoward results; the present case affords evidence that this time may be insufficient. My own rule is *now to incubate the bloods at 37° C. for one to one and a quarter hours in a damp chamber*; the hollow-ground slide is placed in a Petri dish lined with damp filter-paper. To save time, if all is well at the end of twenty minutes the donor is bled, and when seventy-five minutes has elapsed from the time of mixing the bloods, and not before, unless the case is so desperate that the extra risk must be taken, the actual transfusion is commenced. Hitherto all trouble has been obviated, and this I believe to be the only safe method of procedure until such time as reliable high titre Group 3 serums are marketed.

Animal Experiments.

The value of animal experiments in elucidating the causation and indicating the necessary preventive measures in respect of this tragic condition will be apparent. Yorke⁵ found that in order to produce precipitation of injected haemoglobin in the kidneys a dry diet (in rabbits) was essential; if they were fed on a wet diet of greens it did not occur. Blaker and Dodds¹ found that rabbits would pass an acid urine if fed on greens. In one case with an acid urine partial renal blockage occurred with a blood urea of 78 mg. per cent. The rabbit on wet diet had a blood urea of 35 mg. per cent., and passed a red urine without blockage. The factors in precipitation were found to be: (1) An acid reaction (pH 5-6) which converted the pigment oxyhaemoglobin into methaemoglobin, and then probably into acid haematin. (2) Sodium chloride, provided it was in a concentration of not less than 1 per cent.

In paroxysmal haemoglobinuria and blackwater fever there is a similar mechanism with similar pigment casts, but the amount of haemoglobin liberated is smaller, and in these, as in the lesser degrees of transfusion haemoglobinuria, the kidney is generally able to weather the storm.

Therapeutics.

Blaker and Dodds¹ recommend, on theoretical grounds, the exhibition of alkaline diuretics and transfusions of sodium carbonate. It is obvious that what must not occur is an acid, concentrated urine. In my case we tried alkaline diuretics, but, it is probable, not intensively enough. It is sufficient to say that if the urine can be kept alkaline for a few days, experiment has shown that all will be well and no renal blockage can occur.

Finally, the transfusionist must have ample warning, so as to allow the maximum amount of time necessary for cross-agglutination.

Whereas no originality is claimed for anything in this paper, except perhaps the histo-pathology of the liver in this instance, its excuse is to draw attention to the uniformity of the lesions found after death, to the valuable experimental work of Yorke, Blaker, and Dodds, and to show the necessity for a prolonged cross-agglutination test whenever practicable, and so to indicate certain means by which the tragedy of delayed incompatibility may be averted. In conclusion, I desire to thank my colleague Mr. Arthur H. Crook for permission to publish this case.

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VACCINES IN THE TREATMENT OF GONORRHOEA.

BY

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At the venereal diseases clinic of Salford Royal Hospital it was customary during the years preceding 1924 to treat every case of gonorrhoea by a course of detoxicated gonococcal vaccine in addition to the ordinary routine treatment; however, since December, 1923, the vaccine has been discontinued. The vaccine treatment appeared to have a certain definite influence in the prevention and cure of the various complications and in shortening the period of treatment. We have therefore thought it of interest to make a comparison—so far as it is possible—between the results obtained during the years 1922-23 on the one hand and those of 1924-25 on the other.

Routine Treatment.

The clinic permits of the attendance of patients thrice weekly, and the treatment (vaccine excepted) has remained unchanged from 1922 to 1925 inclusive. A urethral smear from each new patient is examined for gonococci, and if urethritis is present the patient is put on a mixture containing 10 grains of potassium citrate, 5 minims of tincture of belladonna, and 1/2 oz. of infusion of buchu, to be taken thrice daily, is supplied with an easily sterilized outfit containing a syringe, and with potassium permanganate lotion 1 in 8,000, and is given a sheet on which are printed all the necessary instructions; after a short period the lotion is strengthened to 1 in 6,000, and later—some four to six weeks after the initiation of treatment—a two-glass test demonstrates the presence or absence of a posterior urethritis. Posterior urethritis is treated by deep irrigation twice weekly with potassium permanganate lotion 1 in 6,000, after the method of Janet, and by prostatic massage once weekly; the irrigation is varied by employing zinc permanganate 1 in 6,000, or silver nitrate 1 in 10,000, and sometimes mercury oxycyanide 1 in 2,000. The progress of the patient is estimated by the two-glass test and by search for the gonococcus, both in films and by means of cultures.

Standard of Cure.

Cure is not accepted unless satisfactory tests are obtained during a period of six months after treatment has been discontinued, and before the final test a return to alcohol is permitted. It is very necessary to define the standard of cure; each doctor has his own criterion, and in the past the cessation of the urethral discharge was often accepted as proof of cure. It is preferable to err on the side of strictness and so avoid the possibility of those lamentable happenings which otherwise sometimes occur.

The Two-glass Test.

The two-glass test is carried out as follows: the patient holds water for three hours prior to examination; he then passes the first specimen, and after prostatic massage the second; both urines are at once centrifuged and examined microscopically, the average number of pus cells in a field being reported. From this count we determine the presence or absence of posterior urethritis: six to seven pus cells to a field, in the second urine, is the figure which we find from experience to indicate approximately the dividing line between a posterior urethritis and one limited to the anterior urethra—that is to say, a figure above this number denotes an extension of infection to the posterior urethra. For a cure the number in the second glass should not be above three, in a few patients four or five, the ideal being *nil* in both specimens.

Vaccine Treatment.

The vaccine treatment, which was added to the routine procedure during the years 1922-23, consisted of two courses of vaccine—the first of ten injections of a residual pure gonococcal vaccine at weekly intervals, and the second, if posterior urethritis developed, of ten injections of a residual mixed vaccine of gonococci, streptococci, staphylococci, and