By this method no portion of the solution can enter the tissues at the point of injection.

It is important that distilled water should be used for making the solution. Tap water produces a fine suspension. We have had no untoward occurrences. There is always a rise of temperature followed by headache and vomiting, and in some cases rigors and diarrhoea.

The condition of the patient is a cause for anxiety at first, but within twenty-four hours all symptoms clear up. In men 0.4 gram, and in women 0.3 gram doses diluted in saline solution have been given.

The intramuscular method has the disadvantage that great pain follows the injection, which may persist for several days, and in some cases weeks. In two cases sterile abscesses occurred at the site of the injection. No culture could be obtained from them, neither could any arsenic be demonstrated. The reaction as regards pain, temperature, headache, vomiting, etc., seems to be much less in women than in men.

In conclusion, I owe much to my house-surgeon, Dr. W. Messer, for his help in assisting me and making notes on the cases. I have also to thank Dr. Stopford Taylor and Dr. R. W. MacKenna for supplying me with some tubes of salvarsan before it was obtainable in this country; also Dr. Moore Alexander for isolating the spirochaete in doubtful cases.

THE CURATIVE EFFECT OF SALVARSAN IN FRAMBOESIA.

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I STATED in my first communication in the BRITISH MEDICAL JOURNAL of February 18th, 1911, page 360, that the injection of 18 cases of yaws with salvarsan at the St. Augustine Yaws Hospital, Trinidad, on January 4th and 11th, was followed by immediate and wonderful improvement. I subsequently injected 3 cases, and I am now (February 18th) able to give the results in these 21 cases. Each received only one injection.

Cured	...	...	13, or 61.9 per cent.
Nearly cured	...	...	3, or 14.3 per cent.
Stationary	...	...	5, or 23.8 per cent.

The shortest period taken to cure was thirteen days, and the longest twenty-eight days.

I find that salvarsan has no effect on yaws tubercles of the nostrils (tubercles situated at the junction of the mucous membrane of the nose and the skin). This failure was noticed in two cases treated by salvarsan and in one treated by serum.

The cases of yaws injected with serum taken from recovering salvarsan cases on the fourth or fifth day all improved for two or three weeks. Some remain stationary, and others have got worse. I believe that if yaws cases were injected with serum every seven or ten days they would be cured with three or four injections.

I injected a goat that had two kids a month old, with 0.3 gram ($\frac{1}{2}$ grains) of salvarsan, and the milk was given to two children in the female ward. Improvement began in the children on the third day, and continued slowly and surely for fourteen days. The goat was borrowed for two weeks, and was sent back to the owner. I intend injecting a cow, and using the milk on a more extensive scale. If my experiment with a goat is verified by others (using more salvarsan than I did) it means a complete overthrow of the theory of Professor Ehrlich, for it must be the salvarsan itself which produces the antibody, and it is probably of the nature of a ferment.

My further experiments with serum are not connected with salvarsan. I put blisters on some yaws cases and used the serum—dose 16 c.cm. for adults—to inject, each case getting his own serum. The object of this experiment was to see if the blistered surface secreted a beneficial substance. I got no results.

I put blisters on some cases cured of yaws by ordinary means, and used the serum on four yaws cases. There was a slight improvement, which did not last for more than a week.

I tried cacodylate of soda, arsacetin, orsudan, atoxyl, and soamin. I find that only orsudan and soamin are of some benefit in yaws. A 9-grain injection (adult dose)

was given once a week. The formula given for soamin is the same as for atoxyl, and I am at a loss to account for the failure of atoxyl, a failure previously recorded by Professor Castellani in Ceylon.

I had salolized capsules prepared by the dispenser and filled with 1 grain of methylene blue and an inert substance. The capsules were gummed and powdered with salol, and allowed to dry. This was done three times. When given to patients and healthy persons, four hours elapsed before the urine was discoloured, so I conclude that absorption takes place in the bowels. I am now trying soamin in these personally tested capsules, and so far as the experiment has gone, it acts well. I will try salvarsan in this way, when a supply comes from England. I suggest the use of tested salolized capsules made with a double end, the small compartment containing 1 grain of methylene blue. On filling such a capsule with a drug, the discoloration of the urine would exactly indicate when absorption began.

It is my intention to try 1 per cent. injections of the hydrochloride of quinine and urea before injecting with salvarsan intramuscularly so as to mitigate the pain by producing local anaesthesia.

SUMMARY.

Salvarsan is the best drug for use in yaws. I have no doubt that this fact has been discovered in every yaws hospital. The experiments in Trinidad have contributed to knowledge in four directions:

1. The serum of cases recovering under salvarsan has been shown to have a curative effect.
2. Nostril yaws tubercles are not affected by salvarsan nor by serum.
3. The milk of a goat injected with salvarsan has a curative effect.
4. Soamin and orsudan are the only organic compounds—excluding salvarsan, of course—that cause some benefit in yaws.

Full details of all my experiments are recorded and communicated to the Acting Surgeon-General of the Colony. My thanks are due to him and others for their appreciation and encouragement. Further experiments will be undertaken.

THE SCIENCE COMMITTEE OF THE British Medical Association.

OBSERVATIONS ON THE OCCURRENCE OF FLUID IN THE ABDOMINAL CAVITY IN PREGNANT RABBITS.

BY

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THE presence of free fluid in the abdominal cavity of the pregnant rabbit has been noticed in the course of research by several observers, but as far as we are aware no special observations have been made with regard to the nature of the fluid present nor to the possible cause of its occurrence. It has occurred to us that some such observations may be of value, especially in relation to the work done by one of us (C. B.) on the pathology of cardiac dropsy.

Relative Frequency.—The relative frequency of free fluid in the peritoneal cavity has been estimated in a series of pregnant and non-pregnant animals:

(a) Non-pregnant: Ten non-pregnant animals were examined, 4 males and 6 females, and although the intestines were moist in all cases, in only 2 was a measurable quantity of free fluid obtained, and in these 2 cases (1 male and 1 female) the quantity was very small, as indicated below.

(b) Pregnant: In 16 pregnant animals examined, we only failed in 2 cases to obtain a measurable quantity of fluid. This gives the following percentages of cases with free fluid:

- (a) Non-pregnant, 20 per cent. (probably is much smaller).
- (b) Pregnant, 87.5 per cent.

Distribution.—The presence of free fluid in the pleural cavity was noted in 3 cases in pregnant animals and in no case in a non-pregnant. In the pericardium a small quantity of fluid was generally found in all cases. In no case was subcutaneous oedema present.

Amount of Fluid Present in the Abdomen.—(a) Non-pregnant: In the 2 cases occurring in the series of 10 non-pregnant animals examined the quantity of fluid amounted to 2 c.cm. and 3 c.cm. respectively.

(b) Pregnant.—In the series of 16 animals, 14 had fluid in quantity varying from 1.15 c.cm. to 25 c.cm.

The series is as follows:

I. 1.15 c.cm.	VII. 3.50 c.cm.	XII. 2.50 c.cm.
II. 14.50 c.cm.	VIII. 2.50 c.cm.	XIII. 2.00 c.cm.
III. 9.00 c.cm.	IX. 3.50 c.cm.	XIV. 1.50 c.cm.
IV. Nil.	X. 8.00 c.cm.	XV. 25.00 c.cm.
V. 3.00 c.cm.	XI. 5.00 c.cm.	XVI. 15.00 c.cm.
VI. Nil.		

We feel justified from these figures in concluding that the presence of free fluid in the abdomen is a more or less general occurrence in pregnant rabbits and not merely a coincidence.

Blood Pressure.—We have examined a series of non-pregnant and pregnant animals with a view to ascertain whether any blood pressure changes were to be noted in animals with free abdominal fluid.

Technique: Anaesthesia.—Ether was used in all cases, anaesthesia being induced with a mask. Tracheotomy was then performed, and the administration of ether continued through an apparatus attached to the artificial respiration pump. Special care was taken to imitate the natural respirations of the animals by careful regulation of the pump, a free outlet of air being provided.

Position.—The animals were fixed to a board in the supine position, care being taken to tie them down loosely so as not to interfere with the venous flow. The head was slightly raised on a small board, the same board being used for all experiments.

Method of taking Blood Pressures.—The following routine was followed in all the cases after the first two or three. First the pressure was taken in the right carotid artery with an ordinary mercurial U tube manometer; then the blood pressure in the left external jugular was taken by passing a cannula down the large auricular vein until the mouth of the cannula came to lie flush with the wall of the jugular vein without obstructing the flow of blood in that vessel. The cannula was then connected with a manometer containing a solution of $MgSO_4$ (specific gravity 1.046) and the pressure in millimetres recorded; the height of the vein above the table on which the manometer stood was then measured and deducted from the pressure recorded. The pressure in the common iliac vein was now recorded in a similar manner by passing a cannula up the femoral vein. At the end of each experiment the pressure in the left carotid artery was again taken.

In a few cases we attempted to take the pressure in the portal vein, but we found this rather difficult, and therefore decided to work it out in a separate series of animals.

The results obtained are indicated below:

(a) Non-pregnant Animals.

No. of Experiment.	Sex.	Carotid Artery B. pressure in mm. Hg.	Jugular Vein in mm. $MgSO_4$ Sol.	Iliac Vein in mm. $MgSO_4$ Sol.	Fluid in Abdomen in c.cm.
1	M.	90	55	83	—
2	M.	60	60	Not obtained	—
3	F.	110	50	85	—
4	F.	58	35	Not obtained	2.00
5	F.	70	37	85	—
6	F.	75	20	120	—
7	M.	65	50	89	—
8	M.	80	45	115	3.00
9	F.	80	39	Not obtained	—
10	F.	77	51	112	—

(b) Pregnant Animals.

No. of Experiment.	Carotid Artery in mm. Hg.	Jugular Vein in mm. $MgSO_4$ Sol.	Iliac Vein in mm. $MgSO_4$ Sol.	Fluid in Abdomen in c.cm.
I	70	42	125	1.15
II	90	50	75	14.50
III	50	56	88	9.00
IV	50	38	74	Nil.
V	90	54	Not obtained	3.00
VI	90	70	96	Nil.
VII	52	53	83	3.50
VIII	70	62	110	2.50

It will be seen from the foregoing that the difference in blood pressure in the two cases is not appreciable, and we feel justified in assuming that there are no pressure changes in the peripheral circulation in the animals with ascites. We believe the same to be true of the portal circulation, but our experiments have not so far enabled us to make a definite statement on this point.

Composition of Fluid in the Abdominal Cavity.—We have examined the blood, the fluid found in the abdominal cavity, and in some cases also the chyle, for total solids.

Technique.—The blood serum was obtained by bleeding the animals from the carotid artery into dried glass tubes, allowing the blood to clot, and centrifugalizing. A portion of the serum was weighed in a dry glass capsule, dried at 60° C., and finally heated to 108° C. and weighed again.

The fluid from the abdominal cavity, which was a practically colourless fluid, was collected into similar tubes with a pipette and allowed to coagulate spontaneously, which it did in all cases in about half an hour. It was then centrifugalized and treated in the same way as the blood serum.

In order to obtain the abdominal fluid for analysis we used only animals in which the blood pressure had not been taken, in order to avoid the possible error of producing ascites by introducing $MgSO_4$ solution into the circulation.

Considerable difficulty was experienced in obtaining chyle in sufficient quantity for estimating the total solids; we first attempted to obtain it from the sub-clavian vein after ligation of the surrounding blood vessels, but failed to obtain undiluted chyle. We also found isolation of the thoracic duct unsatisfactory, and finally obtained the chyle by opening the receptaculum chyli, after all the abdominal fluid had been removed and the animal bled to death.

The examination of the various fluids for their total solid contents gave the following results:

No. of Experiment.	Blood Serum. Total Solids per Cent.	Abdominal Fluid.		Chyle. Total Solids per Cent.
		Amt. c.cm.	Total Solids per Cent.	
IX	6.896	3.50	2.741	—
X	6.324	8.00	2.349	—
XI	7.352	5.00	3.978	—
XII	5.866	2.50	2.254	—
XIII	7.691	2.00	3.115	8.629
XIV	6.738	1.50	4.220	3.738
XV	7.509	25.00	3.226	6.122
XVI	7.433	15.00	4.567	3.550

These figures closely correspond with those obtained in the case of heart disease in the human subject.

We have not yet had the opportunity of comparing the results thus obtained with fluid obtained from non-pregnant animals, as we used the only two cases that have come under our notice for blood-pressure experiments.

The type of dropsy in these animals, therefore, corresponds more closely to that of heart disease than to that seen in disease of the kidney or in hepatic cirrhosis, in both of which conditions the oedema fluid contains much less solid matter.

This conclusion is not at variance with the pathology of cardiac ascites, because, as shown by one of us,¹ in that condition there may be no changes of pressure in the peripheral circulation.

REFERENCE.

¹ Bolton: (a) *Journal of Pathology and Bacteriology*, August, 1903; (b) *Proceedings of the Royal Society, B.*, vol. lxxix, 1907; (c) *Journal of Pathology and Bacteriology*, vol. xiv, 1909.

THE HISTOLOGY OF RHEUMATIC CARDITIS AND OTHER RHEUMATIC PHENOMENA.

BY

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Heart.—In all three parts of the cardiac wall certain inflammatory lesions, which have been called "submiliary nodules," are found. These nodules consist of (a) a groundwork of homogeneous material which gives the staining reactions of fibrin; (b) a more or less defined zone of cellular proliferation, the characteristic cells being large and of a fibroblastic type, with a deeply staining cytoplasm, and from one to six nuclei in which a somewhat loose chromatin skein takes haematoxylin with avidity. They are therefore similar in structure to the larger subcutaneous node so characteristic of rheumatic infection. The shape of the nodule is dependent to some extent on its surroundings, being globular when lying in a loose bed of connective tissue, but fusiform where it is limited laterally, as it is when it develops in the interstitial tissues of the myocardium. In rheumatic lesions of the heart degenerative and necrotic changes are not intense in degree; exudation of leucocytes is moderate and diffuse, mononuclear types predominating.

Myocardium.—Recent work has confirmed the conclusions already stated.¹ The nodules are closely related to coronary arterioles; there are more in the wall of the left than in that of the right ventricle (though in one case the only nodule found was in the wall of the right ventricle) and only once has a nodule been found in the auricular walls apart from a few in contact with the mitral ring. In this case it lay near the base of the Eustachian valve in the interauricular septum. In two cases a nodule has been noted in the connective tissue limiting the *a-v* bundle, and in another case arterial changes in this region coincided with nodule formation at the point of junction between the *a-v* node and the bundle. In one case segmentation has been observed, and in another a close relation between nodule formation and the distribution of intracellular fatty change was seen. On the whole, the muscle cells appear less altered than might be expected, probably owing to the relative coarseness of the staining methods at our disposal.

Endocardium.—Here again recent investigation has merely confirmed observations already recorded.² The points of main interest are the almost constant occurrence of nodules in the deeper parts of the valves, the presence of a diffuse and mild mononuclear leucocytosis, and the ultimate vascularization of the inflamed valve. The endothelium proliferates; the surface cells float off owing to degenerative changes, and the fibrin deposited in this stripped surface—sometimes mingled with leucocytes from the intracardiac blood—becomes permeated with new connective tissue bearing young capillaries.

Pericardium.—The chief facts are that nodules have been found in all cases of active pericarditis, but not in quiescent cases. They have not so far been seen in the parietal but only in the visceral layer, where they are scattered over the cardiac surface. They lie at a varying distance beneath the endothelium, in which proliferation,

superficial degeneration and stripping, fibrin deposit and capillary formation, are seen as in the endocardial endothelium. In the subendothelial tissue a moderate leucocytosis is seen.

The *aorta* has been examined several times but without the discovery of such lesions as have just been described. Mesenteritis and small patches of subendothelial inflammation have been seen, but there has been nothing in these to distinguish them from the similar lesions which occur in most infections.

Arteries, Arterioles, and Capillaries.—In one case the lumen of a coronary arteriole in the vicinity of the auriculo-ventricular bundle was almost closed by swelling of the arterial wall on one side, due apparently to the development of a nodule in its middle coat. Endothelial proliferation with thrombosis has been noted also in the arterioles and capillaries of a rheumatic joint. Coronary periarteritis was alluded to in the paper on myocarditis.

The central nervous system has been more or less fully examined in four cases of chorea.

Here it may be said that widespread chromatolysis is present throughout the cortex, and to a less degree in the optic thalamus and the pontine and medullary ganglia, while in the cord almost no changes were discovered. The pia mater, which has been fully examined both on the convexity and at the base, shows no change beyond intracapillary clotting and an occasional small extravasation of leucocytes. The one is probably due to *post-mortem* clotting and the other to passive hyperaemia.

Only two joints have been available. In one, a large and very definite nodule was found, with others less clearly defined, corresponding essentially with those seen in carditis. It lay just beneath the endothelium, which at other spots was proliferating. Throughout the synovial membrane and extending into the periarticular tissues was a mononuclear leucocytosis; there were further, the vascular changes already noted.

The other organs examined have been the lungs, in which an intense passive hyperaemia was seen, together with a mild bronchial catarrh; the lymphatic glands at the base of the heart, in which passive oedema and congestion were manifest; the spleen and liver; the kidney, in which spots of parenchymatous degeneration have several times been seen; the tonsils, thymus, and adrenals; and the thyroid gland from a case of Graves's disease with chorea, in which the changes peculiar to the former disorder were found. In none of these organs has any kind of interstitial inflammation been seen.

Other types of cardiac infection have been examined by way of comparison with rheumatic carditis. In practically all cases of destructive endocarditis and purulent pericarditis foci of inflammation are found in the myocardium; but in no such case has an inflammation of all three layers been seen. Further, the inflammatory reaction is chiefly characterized by an exudation of leucocytes, usually polymorphonuclear, not by a proliferation of the cells of the part invaded. In one case of protracted cardiac and articular rheumatism, terminated by a lobar pneumonia from which the pneumococcus was readily isolated, two sets of lesions were visible side by side in the heart, and even in the same section—the one characteristic of rheumatic infection, the other a polymorphonuclear focus. In one of these latter pneumococci were demonstrated.

Finally, it may be added that examination of lesions produced by inoculation of animals with micro-organisms said to be the cause or causes of rheumatism is proceeding. A good deal of material has been dealt with, but any statement as to the results would be premature at this stage.

It is my pleasant duty to thank my colleagues at the Bristol General Hospital: Dr. J. A. Nixon, Dr. G. A. Sutherland, Dr. Reginald Miller, Dr. E. H. Kettle, Professor J. M. Beattie, Dr. W. V. Shaw, Dr. F. T. Longcope, and Dr. James Fletcher, for allowing me to use material; and Professor Walker Hall for kind help and for laboratory accommodation.

REFERENCES.

¹ *Quarterly Journal of Medicine*, October, 1908. ² *Lancet*, May 15th, 1909.