EXPERIMENT V.—*Serum of Sheep. Pressure Employed, 8 to 17 mm. Mercury.*

—	Total Proteids.	Serum-Albumin.	Serum-Globulin.	S. A. S. G.
Original serum	7.45	3.81	3.54	1.08
Transudation	5.46	2.73	2.73	1.00

EXPERIMENT VI.—*Serum of Sheep. Pressure Employed, 30 to 37 mm. Mercury.*

—	Total Proteids.	Serum-Albumin.	Serum-Globulin.	S. A. S. G.
Original serum	7.6	5.3	2.3	1.4
Transudation	5.25	2.62	2.63	1.0

EXPERIMENT VII.—*Albuminous Urine. Pressure Employed, 15 to 20 mm. Mercury.*

—	Total Proteids.	Serum-Albumin.	Serum-Globulin.	S. A. S. G.
Original urine (neutralised)...	1.2	0.83	0.32	2.75
Transudation	0.96	0.53	0.43	1.27

HIGH PRESSURES.

EXPERIMENT VIII.—*January 13th. Serum of Sheep. Lasted Two Hours. Pressure Employed, 100 to 140 mm. Mercury.*

—	Total Proteids.	Serum-Albumin.	Serum-Globulin.	S. A. S. G.
Original serum	4.02	2.55	1.47	1.7
Transudation	3.0	2.1	0.9	2.3
Fluid left in bladder	4.35	2.57	1.78	1.44

EXPERIMENT IX.—*January 22nd. Pleuritic Fluid 30 cc. diluted to 50 cc. with 0.75 Na. Cl. Sol. Lasted Two Hours and Five Minutes. Pressure Employed, 160 to 200 mm. Mercury.*

—	Total Proteids.	Serum-Albumin.	Serum-Globulin.	S. A. S. G.
Original serum	2.18	1.13	1.05	1.07
Transudation	1.5	0.9	0.6	1.5
Fluid left in bladder	3.8	1.7	2.1	0.8

These experiments are most crude attempts to imitate the condition in the kidneys. So far as they go, they would indicate that under high pressures serum-albumin transudes more readily than serum-globulin, while with low pressures the reverse is the case. But more careful observations are required before any definite conclusion can be arrived at. The very much more marked reduction in the proportion of the serum-albumin in the urine experiment suggests the possibility that some alteration in the saline constituents of the blood may play a not unimportant part in determining the proportion of these proteids in the urine. This subject is at present under investigation, but as yet no definite results have been obtained.

We are well aware that these observations are imperfect and fragmentary, but we publish them in the hope that others may be induced to study a question of great clinical interest, which requires for its elucidation a much more extensive series of observations than the time and material at our disposal would permit. We believe, however, that the following conclusions may be arrived at:—

1. Senator was right in the conclusion that, in all cases of albuminuria, both of the chief proteids of the blood plasma are present.

2. The proportions of serum-albumin and serum-globulin may vary within wide limits, the quotient of the amount of serum-albumin divided by the amount of serum-globulin being sometimes as low as 0.6, sometimes as high even as 39.

3. In acute nephritis, when blood is absent the quotient is high. When hæmoglobin is present, the globulin is, of course, in excess.

4. As the disease becomes more chronic the quotient sinks, and in the terminal stages of the disease may sink as low as 0.6. This alteration depends upon the condition of the patient rather than upon the state of the kidney, and is probably related to a similar change in the blood plasma.

5. Amyloid disease cannot be distinguished from the ordinary forms of chronic nephritis by the high proportion of serum-globulin as was formerly maintained by Senator.

6. Maguire's suggestion that functional albuminuria is characterised by the high proportion of serum-globulin is not correct.

7. In every case the proportion of the proteids to one another varies much in the course of the day, and in comparing the proportion of these proteids in different cases it is necessary to examine specimens of the mixed urine of the twenty-four hours, and to take into account the nature of the diet.

8. The proportion of serum-globulin is always highest during the night. It falls greatly after breakfast, when it reaches its lowest point in the twenty-four hours. In most cases it again rises in the evening. The precise connection of the alteration in this proportion with the taking of food cannot be considered as definitely settled.

9. Milk diet, as observed by Lecorché and Telamon, has a peculiar effect in increasing the proportion of serum-albumin.

10. The amount of proteids passed appears to bear a tolerably direct proportion to the amount of proteids taken, and, excluding milk diet, the increase of the proteids in the urine on a diet rich in these substances appears to be chiefly due to an increase in the serum-albumin.

11. The variations in the proportion of the albumin to the globulin in the urine is frequently so great that we can hardly believe that it is connected with a similar change in the plasma. The few experiments we have performed would suggest that a high pressure favours the transudation of serum-albumin, while a low pressure increases the proportion of globulin transuded.

FURTHER NOTE ON THE POSSIBILITY OF CURING MYXŒDEMA.

By VICTOR HORSLEY, B.S., F.R.S., ETC.,

Surgeon to the National Hospital for Epilepsy, etc.; Assistant-Surgeon to University College Hospital.

ON February 8th, 1890, I put forward the suggestion in the JOURNAL, p. 287, that attempts to relieve the conditions known as myxœdema and sporadic cretinism ought to be made by transplanting healthy thyroid tissue into the victims of these diseases. The justification of this procedure rested on the remarkable experiments of Schiff and von Eisselsberg.

I only became aware in April, 1890, that this proposal had been in effect forestalled in 1889, by Dr. Bircher, in Aarau. In No. 357 of the *Sammlung klinischer Vorträge*. Dr. Bircher gives an account of myxœdema and cretinoid degeneration, his paper being published on March 5th, 1890. This is not the occasion to discuss Dr. Bircher's views on the subject in general, although they do not altogether harmonise with those generally held in this country, but I wish to draw attention to the valuable results he obtained by the transplantation method in a case of operative myxœdema, or, as it was originally named by Professor Kocher, "cachexia strumipriva."

On page 3404 (12 of the reprint), Case No. 5, he describes the onset of acute myxœdema (as I have termed it) in a female patient from whom unintentionally the whole thyroid gland was removed. Severe myxœdema (cachexia strumipriva) resulting, Dr. Bircher, on January 16th, 1889, transplanted into the abdominal cavity a portion of apparently (*ziemlich*) normal thyroid tissue from a goitre. The effect of this operation was to produce a very marked improvement, so that the patient was enabled to return to work, and the myxœdematous symptoms in great measure disappeared,

only the condition of the skin suggesting the persistence of the malady. Three months later, however, it became evident that the transplanted piece of thyroid had atrophied, as the myxœdema again showed itself and progressed. A second transplantation was made, and again an improvement, and this time greater, resulted, as the patient recovered for nine months, even menstruation returning after amenorrhœa had persisted for over a year. At the present time the symptoms have recurred slightly, but the beneficial effect of the operation was thus indubitably established.

Professor Kocher most kindly wrote to me (May 19th and 31st, 1890) and informed me that he attempted to obtain the same result as early as 1883 by transplanting a small portion of the gland freshly excised from a goitre, but the graft was soon absorbed. Hearing of Dr. Bircher's case, however, Professor Kocher took up the subject again early in 1889 by transplanting in two cases the half of a thyroid gland "in the abdomen," fixing it to the wall by sutures. In both the gland was "aseptically exfoliated" after some time. In three cases he put the gland loose in the abdominal cavity. The results of these cases Professor Kocher has not yet collected nor published, but he has already learnt that one patient has greatly improved since the operation.

Consideration of these results makes it, I think, abundantly clear that this operation should be always performed not simply in cachexia strumpriva—which, of course, with our later knowledge of the function of the thyroid gland, will ultimately disappear—but also in myxœdema and sporadic cretinism. Whether or not it is better to transplant thyroid tissue from a human goitre or a healthy gland from a lower animal, as I suggested in my first note, can only be decided by experience. I cannot forbear from referring to these facts, as tending to confirm clinically in man the truth of the views concerning the function of the thyroid gland which I advanced five years ago, and which, though violently attacked by Munk, have received confirmation from all later experimental observers.

PRELIMINARY NOTE ON THE PROCESSES TAKING PLACE IN THE DIPHTHERITIC MEMBRANE.

By M. ARMAND RUFFER, M.A., M.D. Oxon.,

SINCE the first investigations of Klebs, in 1883, it has been known that a specific bacillus is met with in enormous numbers in certain forms of diphtheria. Löffler¹ isolated the bacillus described by Klebs in six cases of diphtheria, and was able to reproduce typical false membranes by first excoriating the mucous membrane lining the conjunctiva, trachea, pharynx, or vagina of pigeons, fowls, rabbits or guinea-pigs, and then painting the mucous membrane with pure cultures of the specific bacillus he had isolated from cases of diphtheria.

It is a remarkable fact that the bacillus is found in the false membranes only, and not in the organs or blood of persons who die of the disease. Löffler, in his experiments, met with it nowhere except at the point of inoculation. Roux and Yersin² inoculated a number of guinea-pigs subcutaneously, killing one every two hours. After four hours these observers found a marked œdema at the point of inoculation; the number of bacilli increase in this local swelling up to the sixth or eighth hour; some bacilli were enclosed in cells, but the micro-organisms gradually decreased in number, so that when the animal die there were fewer microbes at the point of inoculation than six or eight hours after their introduction. Moreover, the blood and the pulp of the organs of guinea-pigs killed in the manner described were found to be sterile. In one case only did the liver substance of a guinea-pig killed six hours after inoculation give a positive result. The peritoneal liquid, when the injection was made under the skin of the abdomen, and the fluid present in the local œdema alone gave cultures each time. The same observers found that it was impossible to find the specific micro-organisms in the blood or organs of rabbits, in the veins of which a pure culture of the diphtheria bacillus had been introduced. "The spleen of a rabbit, killed after having received 1 cubic centimetre of a pure culture of the diphtheria bacillus intravenously, is removed aseptically, and placed whole into a sterilised tube. After several days in an incubator

at 33° C., no micro-organisms were met with in that spleen." It is easy to find the bacilli six to fourteen hours after the inoculation, and occasionally after twenty-four hours. Notice that the organs of such animals taken out of the body, even when not previously subjected to any processes of heating, etc., form most excellent cultivating media for these bacilli.

It is evident, therefore, that in man and many animals a struggle takes place between the living tissues and the specific microbes, and that, as the result of this struggle, the latter are unable to penetrate into the tissues, and are killed if forcibly introduced into the system.

I have during the last few months obtained evidence that such a struggle takes place in the diphtheritic membrane of man.

The pharynx, larynx, etc., of human patients dead of diphtheria were plunged at once into absolute alcohol until perfectly hardened. Small pieces were removed and soaked for twenty-four hours in a mixture of chloroform and ether, and, if the tissues were very tough and hard, for a like period of time in a saturated solution of paraffin in chloroform at a temperature of 40° C., and for twenty-four to forty-eight hours in paraffin at 42° C. They were afterwards cut in the usual way after embedding in paraffin. The thinnest sections were glued on the slide with a mixture of camphorated glycerine albumen, the albumen coagulated by moderate heat, and the paraffin dissolved with benzole. The slides now passed through absolute alcohol, water and were stained in the usual way with strong alum carmine. After fifteen minutes' stay in a solution of gentian violet in aniline water, the sections were placed in a very weak solution of iodine and water, washed in water and absolute alcohol, rinsed for two to five seconds at most in a solution of three parts of pure xylol to one of aniline, and allowed to remain two to five minutes in pure xylol. If proper care be taken the sections thus obtained are exceedingly pretty, the nuclei and protoplasm of the cells being very distinct, and the deep purple bacilli standing out conspicuously. It is possible in sections so stained to study the position of the bacilli with regard to the surrounding structures.

In thin sections passing through the entire false membrane and the surrounding structures—a section a small bronchus, for instance, when the disease has extended into the lungs—the most superficial part of the membrane, that is, the free edge of the lumen of the tube, is found to contain a most enormous number of specific bacilli, lying for the most part quite free in the coagulated exudation fluid. The micro-organisms resemble short rods of the size of tubercle bacilli, and are often aggregated together into clusters containing hundreds of microbes. So thick is this layer of micro-organisms at times, that on holding the sections to the light a thin violet line is sometimes seen running along the inner margin of the section tube, this line representing the layer of microbes. Scattered among these specific bacilli, more especially in the upper air passages, other kinds of microbes—micrococci and bacilli of various sizes and shapes—are also met with.

If the false membrane immediately below this superficial layer just described be now examined, the number of micro-organisms is found to be exceedingly small, and it will be noticed that not a single bacillus is to be seen in the deeper layers of the false membrane, in the mucous membrane, or the deeper layers of the tissue. The whole process, therefore—as far as the bacilli are concerned—takes place on the surface of the false membrane, and nowhere else.

The space at my disposal does not allow me to describe here the changes taking place in the vessels and tissues of the mucous membrane in cases of diphtheria, nor the mode of formation and structure of the characteristic false membrane. Shortly stated, the latter consists of a reticulated network of fibrin, containing within its meshes a large number of wandering cells, some of which are healthy, whilst others have undergone a distinct process of degeneration. I must draw attention to the fact, however, that the wandering cells present in the membrane are of two kinds, some smaller mono- or multi-nucleated (microphages) and others less numerous, much larger, with a single, clear, vesicular nucleus (macrophages). The latter are found chiefly in the free border of the membrane, and, having wandered into the lumen of the bronchus, may even form a layer in the lumen of the tube.

Many of the leucocytes which have penetrated between the bacilli are quite empty, and contain no micro-organisms in their interior; others, however, especially those present in the layer of the false membrane close to the thick layer of the bacilli previously described, contain in their interior one, two, or more diph-

¹ *Mittheilungen aus dem kaiserl. Gesundheitsamte*, vol. ii, 1884, p. 421.

² *Ann. de l'Inst. Pasteur*, 1889, p. 637.

³ Roux and Yersin, *loc. cit.*