regarded as being secondary to paralysis of the gluteal muscles.

The pathology appears to consist in the coexistence of a vertebral cleft with a hypertrophic condition of the adjacent soft parts, giving rise to pressure upon the cauda equina. Thus Sonnenburg found a deposit of fat beneath the area of hypertrichosis; and Recklinghausen found the cord surrounded and compressed by a myofibrolipoma. In the case which I have just described to you it is probable that the lenticular swelling was of similar nature, and the hypertrichosis usually met with may also be regarded as evidence of the local tendency to hypertrophy.

It remains to be added that there are also recorded examples of sacro-lumbar hypertrichosis in which no other symptoms of spina bifida occulta were present, but that in three such cases of Recklinghausen's a *post-mortem* examination revealed a slight fissure of the subjacent vertebral arches. In Fischer's case, again, a patch of hypertrichosis in the cervical region accompanied the typical sacro-lumbar spina bifida occulta, but no cleft was detected by palpation in the upper area.

Yet another example of this rare disease, which I met with in 1893, illustrates many of its peculiarities:

The patient was a gentleman, 57 years of age, who stated that sixteen years previously he had an abscess of the left foot, from which there came away some bony sequestra. Pain in this foot had continued ever since, occasionally with eruptions on the left great toe. Six months before I saw him two bullae developed on the outer side of the left foot, being accompanied by great pain. The left leg below the knee was distinctly smaller than the right, the calf measuring an inch less in circumference, in spite of previous treatment by massage. The thighs were equally developed upon both sides, and no distinct paresis could be detected anywhere, nor were the rectal, vesical, or sexual functions affected. On the outer side of the sole of the left foot was a healthy scar, with a smaller one situated internally to it. Sensation was markedly diminished in the left leg as compared with the right, and the outer side of the leg was also distinctly more anæsthetic than the inner side. To a much slighter extent the left thigh was less sensitive than that of the right side, and here I was able to satisfy myself that the inner side of the upper part of the thigh was the most anæsthetic. Nowhere was anæsthesia nearly complete, but on the outer side of the left leg there was absolute analgesia to all ordinary stimuli, such as pinching, deep pricking, and the like. Pain was very great on the dorsum of the foot and the back of the leg and thigh, and it was for this pain that the patient sought advice. So far, then, the case resembled one of sciatic neuritis on the left side, but on examining the back we found the condition which is shown in the appended engraving, that is to say, a lenticular swelling, similar to the one which I have already described, accompanied by a curved tail-like process of skin, which was surrounded at its base by a few hairs. It was also obvious that the spinous processes of the first sacral and probably of the last lumbar vertebra were not developed.

Case of spina bifida occulta, from a photograph, showing the lenticular prominence over the sacral vertebra, with a tail-like process of soft tissue about three quarters of an inch in length; at the base of this process were a few fine hairs, some two inches in length. The posterior superior spinous processes of the ilia are indicated by pieces of paper.

That cases of this nature—that is to say, either the cicatrices of old spina bifida or the analogous spina bifida occulta—should be amenable to surgical treatment appeared *primâ facie* probable, and an excellent result was obtained in a case of old spina bifida, which I saw several times with my friend the late Dr. Ross, and which was operated upon and recorded by my colleague Mr. Jones some three years ago.

It appears to me not improbable that the cases mentioned by Athol Johnstone and Holmes as lipomata penetrating to the

spinal canal may have been of similar nature; and Témoin also records the successful removal, from the lumbar region of a child, of a congenital lipoma, which, although it penetrated to the spinal canal, had caused no nervous symptoms.

Chipault records yet another case of Zavaleta's, in which a similar lipoma had penetrated the dura mater, but in which removal was followed by fatal meningo-myelitis.

Lastly, Dr. Shaw and Mr. Bush, of Bristol, have reported recently a most interesting case in which they remained in doubt as to the true nature of the disease, but which not improbably falls into the same category of spina bifida occulta.

The history given by this patient was that, eleven years before being seen, he sustained a wrench of the lower part of the back, from which he dated his illness, although he also stated that for two or three years before the accident he had felt slight dull pains in the popliteal spaces and on the outer sides of the legs and heels. His condition, when seen by Dr. Shaw, was typically that of a pressure lesion of the cauda equina. The lower limbs were weak, especially as regards the hamstring muscles and those of the leg and foot. A perforating ulcer was situated on the ball of the right great toe. Anæsthesia was of the cauda equina type, but presented the peculiarity that the penis and scrotum were analgesic, but not anæsthetic. The muscles except the quadriceps extensor and sartorius showed the electrical reaction of degeneration. Further, there was severe pain in the backs of the thighs and legs, all the symptoms being progressive. The fourth or fifth lumbar spine appeared to be prominent, and at this point there was tenderness on percussion or on the application of heat. An operation performed by Mr. Bush with considerable benefit revealed "a swelling in the middle line, over the lower lumbar spine, which was freely incised, when a rounded cavity covered in with a thin shell of bone came into view. The fifth lumbar spine and lamina had disappeared, and the cavity, which proved to be the dilated spinal canal, contained a solid mass, which was removed. The cauda could not be clearly defined as it was pressed forwards." Microscopically the mass from the spinal canal showed a well-organised blood clot with some fibrous tissue, but no other distinctive structure. My suggestion is that in this case also there had not improbably been either a spina bifida occulta or a true obsolete spina bifida, which had sustained some injury giving rise to hemorrhage at the time of the accident to which the patient ascribed his symptoms.

THE CROONIAN LECTURES

ON

A NEW DEPARTURE IN DIABETES.

Delivered before the Royal College of Physicians of London.

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[*Special Abstract Report.*]

LECTURE II.

THE GLUCOSIDE CONSTITUTION OF PROTEID MATTER.

AFTER a few preliminary observations, Dr. Pavy observed that the molecule of unchanged starch was extremely complex, and that in the process of hydration this complexity was greatly diminished. This was sufficiently indicated by the fact that while the molecular weight of starch was represented by figures between 20,000 and 30,000, that of maltose was 342, and of glucose 180. In the dehydration of sugar into starch in the vegetable kingdom there was not only a subtraction of the elements of water, but a molecular synthesis, leading to the formation of the very complex molecule of the amylose. In the animal kingdom a parallel process occurred with proteid matter. In either case there was, in the process of growth and maintenance of the individual organism, first of all a breaking up by ferment action and chemical action, and then a synthesis by protoplasmic action.

In the first lecture it had been pointed out that from the proteid molecule could be cleaved off a carbo-hydrate molecule. This was equivalent to affirming the glucoside constitution of proteid matter. The group of glucosides comprised bodies of very variable composition; in some, of which salicin might be taken as an example, only the three elements—carbon, hydrogen, and oxygen—were present. In others—of which amygdalin was an instance—nitrogen existed in addition; while in others again, of which myronic acid, obtained from black mustard, was an example, sulphur was also a constituent of the molecule. Another step in the direction of increasing complexity carried us to a body standing in close proximity to the proteids—namely, mucin—

which, as a constituent of connective tissue as well as of mucus, existed extensively diffused throughout the animal system. The researches of Landwehr had shown that, under certain treatment, mucin yielded a non-reducing carbohydrate, which he had described under the name of "animal gum," possessing the formula $(C_6H_{10}O_5)_n$, and that this was convertible into a cupric oxide reducing but non-fermentable sugar, having the composition of glucose $(C_6H_{12}O_6)$, which he called "gumose."

This observation of Landwehr's was of the utmost importance to the subject in hand, since he had thus afforded independent evidence that one complex nitrogenous body, widely present in the organism, was a glucoside. Quite independently Dr. Pavy had, by a long series of researches, been brought to the conclusion that proteid matter had a glucoside constitution. The researches which had led him to this opinion had been carried on in the laboratories founded and maintained by the Royal Colleges of Physicians and Surgeons, and Dr. Pavy expressed in graceful terms his obligation to the wise liberality which had placed laboratories so admirably fitted at the disposal of scientific investigators.

At an early stage of his experiments he had made use of a process for separating glycogen from the liver, which consisted in boiling with potash, pouring into alcohol, and collecting the precipitate. This precipitate, which was considered to be glycogen, was treated with dilute sulphuric

Fig. 1.—Osazone crystals from glucose, showing their acicular structure. (From a photomicrograph.)

acid, which converted it into glucose, and the determination of the amount of glucose gave by calculation the amount of glycogen. The results thus obtained were concordant as long as small quantities of material were used, but from a large bulk of material the quantity of glucose obtained in the final stage was always less than the quantity calculated. The first clue to the explanation of these discordant results was given by the observation that when the action of the potash solution was allowed to continue longer, the amount of carbohydrate eventually obtained was larger. Investigation pursued on these lines showed that the effect was constant, and that the amount of carbohydrate obtained depended upon the strength of the potash solution used as well as upon the duration of its action. Now, if free glycogen or starch had been the source of the cupric-oxide reducing body obtained in the final stage, the treatment of the original material with potash would have produced no effect beyond dissolving the associated nitrogenous material, and no difference in the amount of carbohydrate could have resulted from varying the amount or strength of the potash solution. The conclusion, therefore, was inevitable that the cupric-oxide reducing body took its origin from some other source, and that this was the proteid matter disrupted by the continued action of the potash, with the separation of a carbohydrate body. The mode of preparation of this cleavage product, which was of the nature of an amylose, had been given at the conclusion of the first lecture (see page 1350), and it had been

stated that it was in its chemical and physical properties closely allied to, if not identical with, Landwehr's animal gum obtained from mucin; it had also been stated that under the action of sulphuric acid it yielded a cupric-oxide reducing body. This body could also be obtained from proteid by the direct action of sulphuric acid, as was to have been anticipated from the fact that glucosides are capable of being split up by acids. Dr. Pavy thought it certain that the discovery would have been made long ago but for one fact. This was that the peptone produced at the same time by the splitting of the proteid obscured the reaction of the copper test. The employment of Fischer's phenyl-hydrazine method overcame entirely this source of difficulty. This method applied, with proper precautions, after the splitting action of sulphuric acid had been exerted gave a copious precipitate of an osazone. The form of osazone crystal varied with the degree of action of the sulphuric acid, which could be varied by varying the strength of the acid used and the time for which it was permitted to operate. The less complete the action the more ball-like the form of the crystals and the less speedy was the precipitation. The different forms of crystal probably corre-

Fig. 2.—Osazone crystals from cleavage sugar obtained from egg albumen by direct action of sulphuric acid. $\times 400$. (From a photomicrograph.)

sponded with different forms of sugar. The initial product cleaved off from proteid by the action of sulphuric acid, was more or less widely removed from glucose, but was carried towards it progressively by prolongation of the action. From this osazone the sugar could be separated again by a method devised by Fischer.

CARBO-HYDRATE OBTAINED BY FERMENT ACTION.

The carbo-hydrate could also be cleaved off from the proteid by ferment action: by the agency of proteolytic ferment action the same effect could be produced as by sulphuric acid, the carbo-hydrate liberated being in the form of a reducing sugar. Purified egg albumen, from which all trace of sugar had been removed, was found to yield under pepsin digestion, a product which gave characteristic crystals with phenylhydrazine.

These results were in full accord, it was pointed out, with the view held as correct on other grounds that in the process of digestion and assimilation the proteid of the food was

not absorbed as such, but that every animal formed its own proteid.

The sugar obtained either by chemical action or ferment action was not fermentable by yeast. This was true also of Landwehr's gummosse, obtained from mucin, but, nevertheless, all physiological chemists admitted that gummosse was a sugar. It should also be noted that neither gummosse nor the sugar from proteid produced optical rotation.

THE PART PLAYED BY THE PROTEIDS IN NUTRITION.

Dr. Pavy observed that proof had now been afforded of the incorporation of carbo-hydrates to form proteids, and of the possibility of dissociating the carbo-hydrates again. This dissociation of the carbo-hydrate—its cleavage off from the proteid molecule—must alter the view held of the part played by proteids in nutrition. Liebig's sharp line of demarcation between the flesh formers—the nitrogenous bodies—and the heat producers—the fats and carbohydrates—could no longer be absolutely maintained, since, if the carbo-hydrates were incorporated into proteids, as Dr. Pavy had shown they were, they must be ranked as flesh formers.

CONVERSION OF CARBO-HYDRATES INTO FAT.

Further, carbo-hydrates were convertible into fat. This, again, was easily proved by the facts connected with the growth of yeast in Pasteur's liquid, and in that modification of it in which the tartrate was replaced by nitrate of ammonium. Yeast contained at least 1 to 2 per cent. of fat, and since it could grow in a solution containing no other source of carbon than a carbo-hydrate (sugar) it followed of necessity that fat could be produced from carbo-hydrate by protoplasmic action. Again, proof that fat was produced from carbo-hydrates was afforded by the phenomena observed in the ripening and growth of oily seeds. Before maturity such seeds contained starch and sugar, but no fat; if detached from the plant and preserved in moist air they underwent a process of ripening with the result that starch disappeared and was replaced by an oily fat. Further, to quote the words of Sachs: "There is not the slightest doubt that fat is formed in ripening seeds from carbo-hydrates, particularly starch, since this transformation takes place in the nearly ripe seed, even when taken out of the fruit, when no other material is available under the circumstances for the formation of fat."

CONCLUSIONS.

The conclusions reached so far were to be summed up in the following propositions: (1) Not only can carbo-hydrate matter be hydrated by ferment and chemical action, but when in these conditions of increased hydration can be transmuted by dehydration under the influence of protoplasmic action to substances having more complex molecules—amyloses; (2) in both the vegetable and animal kingdom carbo hydrates take part in the synthesis of proteids; and (3) carbo-hydrates are, under the influence of protoplasmic action, transformed into fat.

THE FALLACY OF THE GLYCOGENIC DOCTRINE.

The acceptance of this position involved the abandonment of the glycogenic doctrine. This doctrine taught that carbo-hydrate matter rendered soluble by hydration in the alimentary canal was carried by the portal vein to the liver, there to be in part stored, and eventually permitted to escape from the liver into the hepatic vein, from which it reached the general circulation, and through it the systemic capillaries, for disposal in the tissues in some unknown manner. The theory was supported by the following contentions: (1) That the liver is more saccharine than other organs; (2) that the blood leaving it contains more sugar than the portal veins; (3) that the blood on the venous side of the systemic capillaries contains less sugar than on the arterial side. All these statements had now been shown to be incorrect. It might indeed be affirmed not only that there was no support for the glycogenic theory, but that it was incompatible with the observed order of things in the animal economy.

THE AMOUNT OF SUGAR IN VARIOUS ORGANS.

Practically the condition of the liver as to the amount of sugar it contained was the same as that of other organs of the body; indeed, the amount of sugar present in muscle might be in excess of that present in the liver.

LIVER.

Amount and Nature of Sugar at the Moment of Death and at Subsequent Periods.

I. Amount and Nature of Sugar at the Moment of Death (Liver removed promptly and frozen).

	Sugar per 1,000 expressed as Glucose.		Cupric-Oxide reducing Power of the Sugar present in Relation to that of Glucose at 100.
	Before Sulphuric Acid.	After Sulphuric Acid.	
Rabbit A	1.601	2.142	75
" B	2.344	3.248	72
" C	1.946	2.828	69
" D	1.664	2.400	69

II. Amount and Nature of Sugar in the Liver at the Moment of Death and at Subsequent Periods.

Rabbit E:			
Liver, frozen	2.000	2.260	88
" a few minutes after death	12.940	12.940	Glucose. 93
" next day	34.340	36.820	
Rabbit F:			
Liver, frozen	0.980	1.060	92
" a few minutes after death	11.550	12.130	95
" next day	33.280	32.530	Glucose.

III. Amount and Nature of Sugar in Livers of Cold-Blooded Animals.

Reptile:			
Tortoise A	1.250	2.170	57
" B	0.852	1.437	59
Amphibian:			
Frogs	1.316	1.724	76

OTHER ORGANS.

Amount and Nature of Sugar in Various Organs of the Body in Various Animals.

	Sugar per 1,000 expressed as Glucose.		Cupric-Oxide re- ducing Power of the Sugar present in Relation to that of Glucose at 100.
	Before Sul- phuric Acid.	After Sul- phuric Acid.	
I. MUSCLE.			
Dog—Tongue ...	2.458	3.727	66
Diaphragm ...	1.662	2.259	74
Heart ...	2.855	4.700	61
Hind leg ...	6.502	9.292	70
Tortoise ...	1.220	1.810	67
Frog ...	0.975	2.330	42
II. SPLEEN.			
Horse ...	1.320	1.634	81
Sheep ...	1.984	2.777	71
Dog (No. 1) ...	1.587	1.827	87
„ (No. 2) ...	2.032	2.777	73
III. KIDNEY.			
Horse ...	1.572	2.575	61
Sheep ...	0.960	1.330	70
Dog ...	1.685	2.229	76
IV. PANCREAS.			
Horse ...	1.463	2.688	54
Sheep ...	0.731	1.388	53
Dog ...	0.812	1.433	57
V. LUNG.			
Horse ...	1.545	2.183	71
Dog ...	3.186	4.870	65
Fœtal pups ...	1.631	1.725	95
VI. BRAIN.			
Dog (a) ...	0.780	1.503	52
„ (b) ...	1.318	1.705	77
„ (c) ...	0.720	1.216	59

Sugar in reality existed as a normal constituent of all the tissues and organs of the body. It was true that in the liver, taken without any precautions to prevent *post-mortem* change, glucose was the kind of sugar met with, but the sugar present at the moment of death, as was shown by the table, had a cupric-oxide reducing power below that of glucose, as was the case with the sugar present in the other structures of the body. In making all such estimations the nature as well as

the amount of the sugar present must be taken into account. The fluid obtained from the organ must be titrated before and after hydration with sulphuric acid. In making such an estimation the organ was extracted with alcohol, and the extract divided into two parts: the sugar in one half was estimated at once with the ammonio-cupric test; the other half was treated with sulphuric acid, and titrated again. If the second estimation gave a higher figure, it was a proof that the sugar in the organ was a sugar differing from glucose, and approaching nearer to maltose. Experiments with cold blooded animals, in whom *post-mortem* changes were slow, gave, as might be seen from the tables, exactly similar results, that is to say, the amount of sugar in the liver and other structures was practically the same.

At the conclusion of his lectures, Dr. Pavy demonstrated lantern slides of ozonones from various sources, among others from certain organs, from beef tea, and from peptonised meat.

REMARKS ON CIRRHOSIS OF THE LIVER, WITH ESPECIAL REFERENCE TO ITS OCCURRENCE IN CHILDREN, AND TO THE MODE OF DEATH IN CIRRHOSIS WITH JAUNDICE.

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I PROPOSE in this paper to narrate certain cases of cirrhosis of the liver in children, in which careful microscopical examinations were made, and to describe and discuss the pathological changes observed.

CASE 1.—F. H., aged 7 months, was brought to the hospital as an out-patient in August, suffering from jaundice. The mother said the jaundice had first appeared about two weeks previously, and, except for this, the child seemed in good health. The child was deeply and universally jaundiced, but otherwise was fat and well nourished, looked lively, and was easily induced to crow and laugh. There was no sign of rachitis; the thoracic and abdominal viscera were normal; the pulse, respiration-rate, temperature, also normal. For the last few days there had been slight diarrhoea, with the passage of green, watery stools. There was no vomiting. The child had always been fed at the breast. A few days later the condition was about the same, except that the diarrhoea had ceased; the urine was found to contain much bile pigment and a little albumen. For the next two or three weeks the symptoms were unaltered, but towards the end of that time the child became rapidly worse. When brought up to the hospital, on September 3rd, an alarming change had taken place. The pulse was hardly to be felt, rate 140; respiration rate 40. There was great oedema of the legs, and marked general anasarca. No ascites. There were purpuric spots in various situations, the largest the size of a threepenny piece on the left anterior axillary fold, and others on the right thigh, on the abdomen, and left foot. The infant lay in a listless state, uttering a feeble cry from time to time; the anterior fontanelle was depressed; there had been almost entire suppression of urine during the previous 24 hours, and a little blood had been passed *per anum*. The mother now consented for the child to be admitted. When lying in bed the little patient became very restless, often cried as if in pain, and drew the legs up on the abdomen; when the mother came to her she took the breast eagerly. The edge of the liver could be felt to be rounded and to come a little way below the ribs. She passed into a semi-conscious state, in which she remained till death, on the following morning, September 4th, at 6 A.M. The respiration and pulse rates became quicker and quicker, the former being 60 to 80, and the latter 160 when last counted. The temperature began to rise at 6 P.M., and steadily rose till it reached 101.2° at death; previous to this there had been no elevation of temperature. A little urine was passed during the night, which contained albumen, bile pigment, and reacted readily to Pettenkofer's test for the bile acids. Careful questioning elicited no history of syphilis in the child's parents; there were no signs of it in either the mother or child, and the latter had never suffered from any symptoms of congenital syphilis. See had never had measles or scarlet fever. The home was a healthy one, and the parents were temperate.

At the necropsy the body was well nourished; there was extreme anasarca, with rather a waxy appearance of the skin; the conjunctivae were deeply jaundiced, the skin less so except over the thorax; *rigor mortis* absent; lungs very bloodless but otherwise healthy; heart muscle substance very pale, but the valves were normal. On opening the abdomen it was found to contain a considerable quantity of dark fluid blood, which was also contained between the layers of the great omentum. In the hilum of the left kidney and in the perirenal connective tissue was a large extravasation of blood; that in the hilum had clotted, a dark clot closely surrounding the renal vein; at one spot the lining membrane of this vessel was dark and blood-stained, and looked softened. As far as I could ascertain this had been the seat of hæmorrhage around the kidneys; the blood did not come from the kidney itself. The aorta, the inferior vena cava, and their large branches were found to be healthy. The portal vessels were large, but I could not discover any other seat of origin for the hæmorrhage, which might, however, easily have been overlooked. The liver weighed 4½ ozs. and came about to

lower border of ribs. Capsule appeared normal, surface smooth and pale. On section it was studded with granules or nodules, the granules being dirty yellow in colour, raised, consisting of the liver lobules, massed together in groups, and separated from each other by pale fibrous tissue which surrounded them. The portal vessels were dilated; the gall bladder was contracted and empty, the bile ducts not obstructed; there was no lardaceous change in the liver. The spleen (1 oz.) was congested and enlarged, and Malpighian bodies somewhat large and translucent; no iodine reaction was obtained. Each kidney weighed 2½ ozs. Capsules stripped easily, leaving a smooth, pale surface. On section the surface was smooth, the cortex was broad (1-3) in relation to medulla, pale yellow in colour, with a streaky appearance. Vasa recta rather full; pyramids pale. The boundary zone was deeply congested, contrasting with pallor of other parts of kidney. The kidneys showed a beautiful example of a more or less general cloudy swelling of the epithelium of the convoluted tubes; otherwise they were normal (Fig. 6). Except that the other organs were rather bloodless, the brain soft, and the dura mater adherent to the cranial bones, no other morbid changes were noted.

To return to the liver. The central parts and the right lobe contained less connective tissue, were softer and more brilliantly coloured; the peripheral parts, and the left lobe were paler and firmer, with more connective tissue. Sections were taken from all parts, and stained in eosin and logwood, methylene blue, picro-carmin, and osmic acid, fuchsin, and methylene blue. In all parts the ordinary structure of the liver and its arrangement into lobules could no longer be distinguished. In the softer parts the field of the microscope is occupied by a finely granular, almost homogeneous material, arranged in a more or less reticular fashion, amongst which lie the remains of the degenerated liver cells, containing pigment granules, minute oil droplets, and often vacuolated. In some fields there are very many, in others very few of these liver cells. In very thin sections the liver cells have almost entirely disappeared, probably partly dropped out in preparing the section, and the character of the intracellular connective tissue appears as a fine soft granular reticulated stroma (Fig. 2). In most parts there is scanty round-celled infiltration, and in a few minute hæmorrhages. In the firmer parts (left lobe and for a depth of about ¼-inch under the capsule) the liver substance was composed of much more fully formed and firmly set connective tissue, with greater infiltration of round cells. In this tissue the remains of the hepatic cells were embedded. The capsule itself was quite thin and of healthy appearance. In the firmer connective tissue close to the older vessels can be seen a few newly formed blood capillaries. In most sections the connective tissue is richly nucleated; these nuclei are irregular in shape but mostly small, as if they had recently divided, and the discovery of a spot under the liver capsule, in which were a number of liver cells whose nuclei were actively dividing, suggests this source for the origin of some at least of the nuclei. Throughout the liver there is an overgrowth of firm connective tissue in the portal areas, and in parts trabeculae extend from them into the liver. There are no newly formed bile canaliculi, the arteries, large and small, everywhere show signs of endarteritis; their lumen being choked by a structureless material containing very numerous large elongated nuclei with prominent nucleoli, evidently arising from proliferation of the endothelial cells. The internal coat appeared to be more or less disorganised, and the elastic membrane of Henle often broken up or unrecognisable. The muscular coat was thickened and its nuclei very abundant, the external coat normal. (See Figs. 3 and 5.) Similar changes were found in the bile ducts, medium sized and small, their lumen being in most cases choked by the products of the disintegrated and proliferated epithelium and their coats thickened. (Fig. 4.) The portal veins were dilated. There were neither micrococci nor crystals of leucin or tyrosin present.

The condition in the liver seemed to consist of an inflammatory exudation of the vessels, with a rapid formation of fine connective tissue throughout the organ, attended with atrophy of the liver cells; the process being more advanced and the connective tissue more completely developed in some parts than in others. The connective tissue appeared to take its origin from the connective tissue of the portal areas and to spread throughout the lobules between the rows of cells from the periphery to the centre; the process being, in short, an acute diffuse cirrhosis accompanied by a very rapid destruction of liver cells. A powerful agent in accomplishing the latter change would be the proliferation of the endothelium in the arteries, which by choking their lumen would