section of these lectures, and in whom an organised concretion existed in the left heart, is the second case of this kind to which I would refer. This lady had suffered certainly from symptoms which had been referred to the heart, but not of an intensity sufficient, as it seemed, to endanger life. Suddenly, after some trifling exertion, she fell and died almost instantly, the globular concretion being carried by the blood-stream into the aorta, and occluding it as effectually as a tight ligature around the vessel.

Lastly, the deposit of fibrine in the heart, in cases of old standing heart-disease, may give rise to peculiarities of symptom reflecting on those of simple cardiac disorder on the one hand, and on those of concretion on the other. In the instance of a girl who had suffered for some years with hypertrophy of the heart and mitral induration, an acute but slight rheumatic attack led to deposition, and to the most extensive deposition I have perhaps ever witnessed. In the course of this case, about four days before death, the mitral murmur disappeared altogether; the pulse at the same time becoming most irregular, and so quick that it was barely to be counted. Without any marked general indications of obstruction from clot, this patient, while sitting up in bed taking drink, exclaimed "Oh dear, how weak I am!" and died instantly from syncope.

Now, in this case, the disappearance of the mitral murmur was accounted for fully at the *post mortem* examination. It was found that the indurated mitral valve was held back by a fibrinous band; while the absence of the special signs of concretion was accounted for by the great size and dilatation of the left cavity. I was not at the time when this case occurred prepared to account during life for the disappearance of the murmur; but in another similar case, I feel that any such difficulty of diagnosis would be greatly removed. There remains yet much to be done in relation to fibrinous deposition in hearts previously and chronically diseased. I have at this moment no further data on the subject; and with this observation I close the history of the symptoms of concretion.

Pathological Changes incident to Fibrinous Deposition in the Heart. Whenever there is deposition of fibrine in the heart, leading to symptoms of obstruction and death, there are produced in other parts certain changes which, though not necessarily organic, are deserving of consideration.

The condition of the *lungs* first calls for attention. The lungs are always changed; but the change varies from two of the widest extremes—i.e., from the extreme of bloodlessness to the extreme of congestion. These distinctions depend upon the position and size of the obstructing body. When the concretion is on the right side, and is of such size and in such position as to check the circulation to the lungs effectually, the state of the lungs is then very uniformly the same. The organs are inflated, blanched almost to pure whiteness, and bloodless. In some instances, to these signs emphysema is added: then the pleural membrane is seen elevated in bead-like rows over a considerable tract of the external surface. In children dying of acute hyperinosis, this emphysematous condition is, according to my experience, always present, and, as a general rule, present in the most marked degree. If the concretion, still supposing it to be on the right side, be so small or so placed that it will allow a current of blood to pass to the lungs, the normal force of the current being nevertheless considerably reduced, then the lungs, instead of being blanched, are congested throughout, and even condensed in depending parts.

When the deposition is on the left side of the heart, whether it obstruct much or little, and whether death be sudden or prolonged, the lungs are always congested. But, in prolonged cases, there is often more than congestion; there is effusion, œdema, sometimes exudation of blood itself, profuse secretion into the bronchial passages, and condensation of structure in depending parts amounting to hepatisation.

The *pleural cavities*, in all forms of deposition, sometimes contain serum of a pale straw colour, which varies in amount, but does not extend to a sufficient amount to cause compression of the lung-structure. In one example, I observed that serum exuded into the pleural cavity coagulated on exposure to the air, a little fibrine having been thrown out with the serous fluid.

The *pericardium* usually contains serum in excess; but, again, not in sufficient excess to stop by its pressure the action of the heart. When this fluid is cleared away, one is often struck, especially in examining the bodies of children who have died of concretion laid down in the right auricle, with the peculiar appearance of the heart: the auricle, from distension, is as large, or is even of larger size than the ventricle; the veins of the heart superficially are distended almost to rupture; and

the whole appearance of the organ indicates the intensest congestion.

The condition of the *large veins*, and of the parts below the heart, the *liver*, *kidneys*, and *spleen*, in cases where the concretion is on the right side of the heart, is one also of extreme congestion. In chronic cases, such as those related in a previous page, where the obstruction extends over weeks or months, there may be œdema of the lower parts of the body, or even effusion of fluid into the peritoneum. In a case seen by Mr. McNab, in which a child died with the signs of concretion on the right side, and in which the *post mortem* examination showed a firm concretion in the right auricle, with pathological appearances in the lungs such as have been so often mentioned—viz., bloodlessness and whiteness of texture—there was found intussusception in five portions of the small intestine, in one portion to the extent of three inches. Mr. McNab suggests that this intussusception may have been due to spasm arising from the deficiency of arterial blood in the intestine—a very probable hypothesis. The symptoms of concretion in this infant were observed first on Monday; its mouth then felt cold to the nipple of its mother; and it continued cold and apparently insensible to everything till Wednesday, when death occurred. I have not in my dissections met with any such condition as is here described in cases of death from fibrinous deposition.

The concretion being on the left side of the heart, the congestion of the abdominal veins and organs is less determinate; for in fact the lungs receive a large supply of blood, and the congestion is shared by the two circulations, pulmonary and systemic. In very prolonged cases, nevertheless, the œdema and other indications of central obstruction may have an extensive manifestation in the parts below the heart.

The *brain* is always congested when there is concretion on the right side, and this congestion may extend to effusion beneath the arachnoid or into the ventricles; but again the fluid effused is always small in quantity. Not unfrequently the sinuses of the brain will be found containing separate tubular deposits of fibrine. When the concretion is on the left side, the brain is also congested, as a general rule, but to a less extent.

It must always be a matter of care, in summing up the pathological appearances incident to concretion, not to confound these with conditions pertaining to other coincident forms of disease, nor to mistake secondary for the primary causes of the changes of structure which are presented by the scalpel. In the brief history I have given, I have kept this caution in view, and have intentionally reduced the description to the narrowest bounds, that there may be no chance of stepping beyond the simple and the true.

Original Communications.

EXPERIMENTAL EPICRISIS OF SOME LATE RESEARCHES ON LIVER-SUGAR.

By J. L. W. THUDICHUM, M.D.

THE discussion which has lately taken place at the Royal Society, of a paper by Dr. Harley, in which the views advanced some time ago by Dr. Pavy, and noticed at length in this JOURNAL, relative to the glycogenic function of the liver, are controverted, recalls to my memory some experiments which I made in the early months of 1859, with a view of testing the correctness of Dr. Pavy's chemical proceedings and physiological conclusions. The result of these experiments is adverse to the opinion of Dr. Pavy, and in accordance with that of Dr. Harley, and consequently confirmatory of the doctrine of the glycogenic function of the liver, as generally admitted before the publication of Dr. Pavy's paper. My experiments have, moreover, afforded me an opportunity of ascertaining the sources of fallacy in at least two of Dr. Pavy's modes of proceeding, and have taught me the conditions under which opposite results may be obtained by the same experiment with the same proceeding—a fact which (as I am informed) was left unexplained by the late discussion.

A dog of fifteen pounds weight, which had for several days been fed upon tripe exclusively, was narcotised with puff-ball, and deprived of a small piece of his liver. This, without loss of time, was pounded with an equal amount of caustic potassa, without the addition of water; and the pale reddish magma was filtered through asbestos. The first filtrate, brought into

an alkaline solution of copper, gave an abundant red precipitate of suboxide of copper, evidencing the presence of sugar. Every drop of the filtrate which passed during the next hour yielded the reaction. After that, the filtrates ceased to show sugar. The mixture on the funnel had been mixed with water and stirred, and had assumed a dark red colour, having been of a pale flesh-colour before.

A second piece of the same liver was exposed to the air for fifteen minutes, and then treated like the first. It exhibited the presence of sugar for one hour, after which the reaction ceased.

The rest of the liver was placed in water boiling in a copper pan. The extract afterwards yielded sugar and glycogenic substance. No leucine was present in this extract.

In the second experiment, a dog of twenty-one pounds weight was narcotised by a blow on the head. One entire lobe of the liver was quickly pounded with potassa; and, after incorporation of the two substances, some water was added to the thick magma. It was observed during the pounding and trituration, as well as during the admixture of the water, that the temperature of the mixture rose so considerably that the hand, which was placed to the outside of the thick Wedgewood mortar, felt it to be quite warm. The filtration of this mixture was difficult, owing to the asbestos being too fine. The first clear filtrate was only obtained after half an hour had elapsed, and contained no sugar.

To one ounce of the mixture, ten grains of pure grape-sugar were now added. The filtrate, after twenty-four hours, did not at first give any reaction with copper solution; indeed, none at all could be perceived in a test-tube. Only after prolonged standing of the test in a china dish, the merest trace of red deposit could be distinguished in the bottom of the dish after the fluid had been cautiously decanted. The ten grains of sugar had so effectually been destroyed in the mixture, that certainly not one-thousandth part of them was left over.

The rest of the liver contained little glycogenic substance, but no leucine.

The third experiment was made upon a dog fifteen pounds in weight. The abdomen was opened while the animal was under the influence of puff-ball. The mixture of liver and potash became again very warm, was mixed with water, and quickly filtered through cotton by the help of air-pressure, upon the principle of Beart's coffee-machine. The filtrate showed no reaction for sugar, but assumed a violet colour.

The first experiment showed me that, when a liver containing sugar is treated with caustic potassa, under circumstances preventing any rise of the temperature of the mixture, the sugar, under the influence of caustic potassa and the oxygen of the air and water, is rapidly destroyed.

The second experiment showed that the destruction of sugar, under circumstances favouring a rise of the temperature, is more rapid still; the presence of sugar being, of course, assumed or allowed. It also showed the rapid destruction of sugar, under the influence of potassa and air, at the ordinary temperature.

The third experiment exhibited the influence of a raised temperature alone in destroying (hypothetical) sugar mixed with caustic potassa. So short a time was passed in the experiment, that, even allowing some influence to the oxygen dissolved in the water, the influence of the oxygen of the air, though not excluded altogether, must have been limited.

No doubt, in the second and third experiment, the proof of sugar having been originally present in the liver is wanting. But the first experiment made me so well acquainted with all the conditions which are essential for finding or missing any sugar in the liver, by employing potassa as a reagent, that I was quite satisfied of the correctness of the conclusion, which caused me at once to give up all further experiments on this subject as lost labour; namely, that *no experiment can be admitted as proving the absence of sugar from the liver, in which the contact of that organ with potash, air, and water, at the ordinary or any higher temperature, has not been avoided.*

The behaviour of grape-sugar with almost any alkali will for itself substantiate that proposition. A solution of caustic baryta and grape-sugar, on standing, is gradually transformed entirely into one of glucate of baryta. A mixture of caustic potassa and grape-sugar, when only heated to 60° or 70° centigrade (140° or 158° Fahrenheit), becomes brown, and smells of caramel; and the sugar is entirely transformed into glucic and melassic acids. Grape-sugar fused in the water-bath reacts so violently with solution of caustic potassa, that frequently a portion of the mixture is projected out of the vessel employed for the test. Caustic alkali, then, of itself, without the inter-

ference of oxygen, is most hostile to grape-sugar, and appropriates and transforms it with increasing violence, the higher the temperature under which they meet.

A mixture of grape-sugar and caustic potassa is very liable to be attacked by the oxygen of the air, directly and indirectly. Such a mixture, when exposed over-night, loses from 30 to 40 per cent. of its sugar, as was proved by Traube, in some experiments made for another purpose. But when to the mixture is added a body having more direct affinity to the oxygen of the air than sugar, but less when that oxygen is once in a bound condition, and therefore easily parting with it, then the oxidising action of the air becomes most fatal to sugar. Such a body is indigo, which at the same time admits of making the experiment visible. It rapidly yields oxygen when dissolved in the alkaline mixture, and is reduced, becoming colourless; but the air restores oxygen and colour to the surface, which again passes it to the sugar below. Not until the whole of the sugar is oxidised, does the fluid resume its blue colour. The indigo here acts as a mediator between the oxygen of the air and the sugar, by transferring it from one to the other. A precisely similar agent of transfer is the red colouring matter of the blood contained in the liver. When mixed with the alkali, it becomes pale, is reduced; something (sugar, when present, at all events) is at the same time oxidised. The addition of water containing oxygen, the contact of the air itself, restores the dark red colour, immediately to be lost again in the lower strata of the fluid. Ultimately the fluid remains dark; all oxidisable matter is destroyed. The sugar of the liver is not only destroyed by the direct agency of air and caustic potassa, but also by the oxygen, which the red colouring matter of the blood has a remarkable power of binding and transferring.

When I applied these considerations to the experiment of Dr. Pavy, in which he injects a solution of caustic potash (in water, not stated to have before been freed of oxygen) into the liver of animals (showing the temperature of 37° centigrade, or 99° Fahr., and being saturated with oxygen or filled with blood containing it in a loosely combined state), I was forced to the conclusion, that any sugar which might be present, would assuredly be oxydised and destroyed at once. The hurry with which Dr. Pavy found himself obliged to operate, to avoid finding any sugar, has its ready explanation in the rapid decrease of the temperature which the liver does experience when the abdomen is opened. The higher the temperature at which sugar, potash, and oxygen meet, the more rapid and complete is the destruction of sugar; if the liver is allowed to get a little cool before injecting the potash, sugar is found, because it has not all been destroyed.

The facility with which sugar in alkaline solutions attracts oxygen from the oxides of metals, points the same way. The reaction with copper has become the test for grape-sugar. Acetate of copper, peroxyde of lead, nitrate of suboxyde of mercury, corrosive sublimate, nitrate of silver, chloride of gold, trisnitrate of bismuth—surrender a portion or the whole of their oxygen to grape-sugar in alkaline, neutral, or even acid solutions. The avidity of grape-sugar for oxygen, under a great variety of circumstances, is really astounding.

The potash-test having been the basis of Dr. Pavy's conclusions, and being now proved to be fallacious, the conclusions themselves, in so far as they are derived from the analysis with potash, are not any longer valid. The reverse of Dr. Pavy's results has moreover been obtained by means of my own; and now by the much more extensive experiments of Dr. Harley, made with Dr. Pavy's own methods. The experiments in which freezing and citric acid are employed respectively, I have not repeated. But this I have experienced in some preliminary tests, that alkaline citrates have so strong an affinity for the oxygen of the air, that red suboxyde of copper, lying at the bottom of a test-tube half filled with alkaline citrate, after exposure to the air for some days, becomes oxydised again, and dissolves with a blue colour in the previously colourless fluid.

I must confess that I am unable to comprehend the meaning of the freezing experiment; but, leaving aside speculation, there is in Dr. Pavy's proceedings following the freezing much reason for distrusting that experiment also. He met with great difficulty in filtering his alkaline solutions of liver, and therefore neutralised them with sulphuric acid before filtration, filtered them by squeezing through flannel, and then again made them alkaline. The mixture thereby not only became enormously bulky, but was for a length of time exposed to the air under a variety of circumstances; Dr. Pavy apparently taking it for granted that, when liver and potassa were once incorporated, the rest of the operation could be completed at leisure, as sugar would not any longer be formed. But, in

absence of the guarantee that none would be destroyed, and in presence of evidence that much is actually destroyed under those conditions, his very security makes it doubtful whether he employed even that moderate speed which his method permitted.

For the repetition of Dr. Pavy's, or other similar experiments, I can recommend a small Beart's coffee machine, and the cotton filters sold with the machine, as the speediest and best contrivance for effecting quick filtration.

As the result of many experiments, Dr. Pavy found that there was no sugar present in the liver; but, on the other hand, he gives as the result of sixty observations, that sugar is only found to the extent of the merest trace in the blood of the right side of the heart, under a natural or ordinary condition, during life. Even this result, although of a positive nature, and speaking against his conclusions relative to the liver, is not without objections, based upon the mode of analysis employed. He defibrinated the blood, probably by stirring, treated it with spirit, and pressed through flannel. The residue of the evaporation was tested with Barreswil's solution. Blood to be analysed for sugar, in order to find a maximum, must be analysed much as for urea; it must be allowed to flow directly into absolute alcohol, and afterwards the additional precaution must be taken of removing its alkalinity when the filtrate concentrates on the water-bath, otherwise much sugar is necessarily destroyed.

I had formed the above positive opinions and conclusions on Dr. Pavy's experiments many months ago, as many friends can testify, who were either present at one or the other of the experiments, or were in conversation informed of my conclusions. For this reason, my results and reflections, which were obtained quite independently, may be considered a strong confirmation of some of the propositions of Dr. Harley, as contained in the published abstract of his paper.

ON YELLOW FEVER.

By GEORGE BROWNING, M.D.

[Read before the Harveian Society, February 16th, 1860.]

THE importance of the subject which I have selected for this paper will at once be conceded, occupying as it does a foremost rank in the catalogue of epidemic diseases, whether we consider the various countries in which it is most prominent, or the havoc and death which have prevailed, and which still prevail, in those subject to its fearful visitations.

The subject of epidemic diseases generally seems scarcely to have claimed from individuals or from governments that high consideration which their importance demands; for, although "they are portentous things unto the climate that they point upon", they may sometimes render "fearful objects so familiar" that we seem not to feel the danger, in the general distress by which we are surrounded.

There doubtless is, in epidemic seasons, a little more activity in the general pulse. Authorities meet and discuss quarantine and other grave questions. The subject of free ventilation may be agitated; the importance of large supplies of pure water may be admitted; dust-carts and scavengers may be called so early into requisition, that the potent rays of the sun may not yet have disengaged any noxious odour; drains and cesspools are forthwith to be only imaginary nuisances; and a ruthless enemy is so assailed in every quarter, that we might fancy a hasty retreat being beaten to some mountain height.

In like manner is the public mind aroused to sympathy at intervals by some melancholy and startling announcement; as when the steamboat boilers explode, and instantly human fragments, even by dozens, are scattered in the air, and death in terrible form meets the eye; or as when a ship founders, or is wrecked at sea, and hundreds perhaps are doomed to measure the interval between dismay and dread reality by minutes or hours.

Social reforms are yearly agitated, and glaring evils boldly exposed; whilst there is too much reason to believe that in each case, after a little time, we become apathetic. The thousands who have been swept off by an epidemic rest quietly in their graves, and occupy a page in Death's statistics. Accidents by sea and land may have the doubtful light of executive investigation thrown upon them; and many of the social evils may be reproduced another year, to undergo the national purification of a vaunted reform!

As early as the days of Sydenham, down to those of modern writers, different forms of epidemic diseases have been attri-

buted to what has been designated an epidemic or pestilential constitution of the air, to which may be added a certain susceptible state of the body; but, as yet, little seems to be definitely known of this peculiarity, which in a great measure is capable of causing epidemic diseases. Speculation, whilst it might attempt to remove the veil and solve the mystery, would still leave us in the suspension of doubt and the mist of uncertainty. We know, however, that one effect is to produce malignant fever, in one or other of its varieties; and upon that called the yellow fever I now purpose to make a few general remarks.

This fever is generally met with in low and level localities. Some parts of the West Indies, and certain parts of North and South America, present all the natural and geographical advantages necessary for the origin and spread of this disease. Sometimes it stretches across the Atlantic, and rages in Cadiz, Seville, Barcelona, and Gibraltar; having visited Lisbon and Leghorn, spreading extensively in this last city, in 1804.

The more elevated parts of the West India Islands are exempt from this disease. Thus, some towns in Jamaica, at an elevation of 2,000 feet, are healthy, as well as the higher parts of St. Domingo. Major Tullock reports that, at an elevation of between 600 and 700 feet, at Dominica, he could not secure a healthy position; whilst, at an elevation of from 2,000 to 2,500 feet, his men were likely to be wholly exempt from this disease, or to encounter it in so very modified a form that the mortality from all causes will not, in the average of a series of years, materially exceed that to which an equal number of European troops would be subject in their native country.

Humboldt, again, has assigned in Mexico an elevation of more than 3,000 feet for the required exemption. Until recently, the river Amazon formed its boundary south of the equator. Within the last few years, it has prevailed at Rio Janeiro, Pernambuco, and other contiguous cities. It has rarely invaded the Pacific coast, and on these occasions it has only visited Panama and Callao. Of late years, the cities in the northern portion of the United States (if we except Philadelphia in 1853) have been almost exempt from yellow fever; whilst some of the cities and surrounding country, in some of the southern States, have yearly visitations.

Unlike cholera, small-pox, and other epidemic diseases, the yellow fever has geographical limits, beyond which it does not appear, and only at intervals at some of the places within these limits. In the West Indies, and in some parts of North and South America, it has its most permanent abode. Thus we find that it extends about 44 degrees north and 23 degrees south of the equator, and from about the 60th to 97th degrees of west longitude, exclusively of those points in Europe where it occasionally prevails, embracing altogether a large portion of the earth's surface.

Not to attempt any historical review of the date and order in which yellow fever has prevailed in different parts of the world, I may observe that, so far back as 1692, the fever was imported into Boston from the West Indies; and in 1699, it appeared in Charleston, South Carolina, and in Philadelphia, it being only a few years after the settlement of the last named city, and the population numbering at this time only a few hundred souls.

Having glanced at the topography of the disease, I may pass on to the predisposing and exciting causes, some of the peculiarities of the mode of invasion, its symptoms, and termination.

Long continued heat and drought are atmospheric conditions favourable to the origin and spread of yellow fever; although, in some of the epidemics in British Guiana and some parts of the West Indies, these auxiliaries are not always found to exert an influence on its development. Thus, observes the late Dr. Blair of Demarara, the year 1853, during which the very beds of the navigable canals were deeply cracked from drought, was not followed or accompanied by any invasion; and the epidemic was long on the decline before the dry season of 1845 and 1846. It is also remarked by another writer, referring to the West Indies, that, in the majority of instances, the most severe attacks of the disease have occurred in the cold season, and not unfrequently when the weather has been peculiarly agreeable as regards sensation, and, it might be supposed, not unfavourable to health. These conditions do not apply to the localities generally where I have witnessed the origin and spread of the disease, although I have known them to obtain after it has become epidemic.

Predisposing Causes. An important predisposing cause, not to be lost sight of in this enumeration, is the constitutional condition induced by previous residence in high latitudes and cold climates. Thus the percentage of mortality gradually de-