LETTSONIAN LECTURES

ON

THE PATHOLOGY AND TREATMENT OF SOME DISEASES OF THE LIVER.

Delivered before the Medical Society of London.

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LECTURE I.—THE LIVER AND ITS NERVES.

WHEN I accepted the honour of delivering to the Medical Society the Lettsonian Lectures, I had hoped that time would have permitted me fully to work out the subject on which my mind rested; but I find that I must ask the indulgence of the Society. The pressing duties of professional life have left to me only fragments of time, and I am compelled to arrange thought and work in a manner that very imperfectly satisfies my wish. It had been an easier task to choose some isolated disease, and to present it fully before the Society; but, in lectures designed to commemorate the liberality of a physician such as Dr. Lettson, the practical is more appropriate than the theoretical, and that which is of every-day occurrence is more suitable than the rarer phenomena of disease. I trust that the consideration of some pathological questions connected with such an important organ as the liver may interest the members of the Society, and be suggestive of useful practical thought. I may be excused in the title that I have proposed for my lecture; for that of the liver and its relation to the nervous system is too wide in its significance, whilst that of the liver and its nerves is too contracted in its meaning.

It is greatly to be regretted that the tendency of modern medical practice is often to separate so much the diseases of one organ from those of another, and to dissociate, as if organs had independent action, and could perform fully their functional requirements with very little connexion with other parts; whereas there is the closest unity in the arrangement of the structures of the whole body, and especial means are used to bring one portion of the organism into sympathy and intimate relationship with another. The two great means by which this living union is rendered effectual are the blood and the nervous system: the former the medium by which fresh supplies of nourishment are afforded, or effete materials carried away from the ultimate structures; and the latter the agent which guides and controls and harmonises the mutual workings of separate parts.

It is scarcely necessary to advert to the position which the liver occupies between the stomach and absorbing intestinal mucous membrane and the lungs and the heart. It receives the venous supply from the whole intestinal tract, and eliminates from the blood hydrocarbons in the secretion of bile; whilst at the same time it reacts upon the constituents of the blood in a manner which modern physiological chemistry has not yet made known. The liver is, we believe, a vascular gland, as well as the source of bile. But the liver itself is in a great measure under the control of nervous centres; and to this I would ask for a few moments the attention of the Society.

It is not known how glandular structures are affected by the nerves, whether simply by regulating the quantity of blood which is sent to the gland, or by some more direct influence upon the secreting cells; but the action upon the vessels does not fully explain the phenomena we occasionally observe. It is not merely a change in the quantity, but in the character, of the secretion, that the nervous influence is capable of producing. A sudden fright or intense emotional excitement has rendered the secretion from the breasts absolutely detrimental to the infant; the secretion from the kidneys undergoes immediate change, or may be checked, by profound nervous impression; under great emotional excitement or distress, the appetite is lost, and food does not digest if placed in the stomach; and, whilst it has long been recognised that the mind has a causative relation in the production of acute yellow atrophy of the liver, a state in which the glandular function is well-nigh stopped, still the lesser changes upon the liver are continually overlooked. In these days of intense mental anxiety—of constant strain upon the thought of men—of wrestling as if for life in the competition and struggle to obtain wealth—there is an influence, and that of a deleterious character, upon the functions of organic life, and the largest of the glands is often impaired in its integrity. Reference is not made to hepatic disturbance from excesses, in which the secretion of bile is altered, the countenance becoming sallow, the tongue furred, the excretions changed. In the hepatic disturbance to which I now refer, there is no sallowness, but a distressed and anxious countenance. The bile is excreted as in health; but the liver is not doing

its work properly; the general nutrition of the body is interfered with; the patient is unequal to ordinary exertions; the ordinary duties of life become burdensome; the sleep is unrefreshing; the appetite is lessened; the pulse is compressible; there may be in some a gouty dyscrasia produced; in others there is a transient glycosuria; the liver is disturbed by an overstrained nervous system. This condition is not diabetes, neither does it present the symptoms of that disease: there may be no thirst, no excess of urine; nor is the condition persistent. It has often surprised me how frequently, in some of the forms of atonic dyspepsia, this evidence of changed hepatic function is observed; and it is important, as directing us not only to the cause of the malady, but it suggests the curative means—not so much the administration of drugs as the diminution of that which induces nervous exhaustion. To forget the cares of life, to take off the burden, to seek the mountain-top and the wild moorland, far from the arena of strife and vexation, is the best remedy for many of these cases of hepatic indigestion. And, if these more effectual means cannot be used, at least the long hours of mental effort may be lessened, and time allowed for nervous energy to be restored. Sometimes a sudden nervous fright will produce severe jaundice, as in the case of a poor out-patient of mine at Guy's Hospital. A washerwoman, having left her room for a few minutes, returned to find all the clothes in flames. Her fright was followed in a few hours by jaundice. There was no pain, no febrile excitement; but, as the mind became composed, and after a few days' interval, the jaundice disappeared. If the distress be less sudden, but more prolonged in duration, there is also disturbed action of the liver. It would be a great mistake to treat the liver in these instances. "It is only the liver out of order," is a common expression, but generally incorrect. More frequently the hepatic disturbance is only the expression of a general state, and is relieved by general means. But, before entering further upon pathological considerations, it may be well to inquire what are those nervous connexions whereby this close bond is maintained and these symptoms produced. The pneumogastric nerve, the vaso-motor nerve, and the ganglionic centres by which these nerves are brought into union, deserve our attention.

[The lecturer then spoke of the distribution of the pneumogastric and phrenic nerves, and their union with the semilunar ganglia and with the splanchnic nerves. Dissections and diagrams were shown.]

Division of the pneumogastric nerve does not produce such marked effects upon the liver as upon the stomach and the lungs; but this subject requires further investigation. In a case of cancerous disease of the breast and of the vertebrae, under my care some years ago in Guy's Hospital, and in which paralysis and atrophy of half of the tongue was produced by a cancerous growth pressing upon the ninth nerve, there was also direct pressure from a similar growth upon the left eighth nerve, the pneumogastric; and there was great wasting of the left lobe of the liver, but no cirrhosis, and no fatty degeneration of the gland. Claude Bernard, in his *Leçons de Physiologie*, published in 1855, drew attention to most interesting facts connected with the pneumogastric and the functional activity of the liver. These experiments are well known, and have been fully illustrated and further developed in the observations of my colleague, Dr. Pavy. These investigations were the subject of the Lettsonian Lectures in the year 1860, and it is not necessary that I should do more than allude to them. Bernard showed that in diabetes there was an increase in the functional activity of the liver; and he produced an artificial diabetes by puncturing and irritating the floor of the fourth ventricle, or by galvanising the pneumogastric in the neck. His explanation was, that the vaso-motor nerve upon the hepatic vessels was affected in these experiments; that the vessels became dilated by the paralysis or lessened power of these nerves; the quantity of blood in the gland increased, and sugar was produced. Dr. Pavy has indicated still further that division of the superior cervical ganglion, and Cyon that excision of the last cervical or the first dorsal ganglion, have a like effect. It appears to be shown that this action upon the liver is one of lessened nerve-power, and the symptoms of disease confirm the statement. We have already alluded to the fact of transient glycosuria being a not unfrequent symptom in atonic dyspepsia; and the same diminished power is shown, as we have several times observed, in the presence of considerable quantities of sugar in the urine for short periods in atonic gout.

A year or two ago, a gentleman about sixty-five years of age consulted me for chronic gout. The urine was highly albuminous, but I also found that there was a very considerable quantity of sugar present. After a few days the sugar entirely disappeared; there was no excessive thirst; no large appetite; the quantity of urine was not excessive, nor was there the progressive wasting of diabetes. The gouty disease of the kidneys continued, although for a time relieved. Again there was a transient return of sugar; but several months afterwards bronchitis supervened—another indication, with him, of weak-

ness of the nervous system, and especially of the pneumogastric and its associated vaso-motor branches. The bronchial affection led to a fatal termination. It may be stated that the urine was of high specific gravity; and, unless there had been an evident gouty dyscrasia, the presence of albumen might easily have been overlooked. And a deeply painful instance of disease, which very recently I saw in consultation with several professional brethren, bears upon the same association of disease. A gentleman, in active practice till two or three weeks before his death, had been the subject of chronic gout, with a very sluggish condition of the colon, but with ordinary aperients the bowels had acted till one week before his death; then severe pain in the region of the cæcum came on, with constipation and flatulent distension of the abdomen. The colon was enlarged, but pain soon ceased; and it seemed as if the sigmoid flexure had bent upon itself and thus led to obstruction. The liver was felt just below the ribs, and the surface was irregular, but no defined tubera could be made out; there were no enlarged glands; nothing could be felt in the rectum; and a tube could easily be passed by a surgical friend eighteen to twenty inches without pain, which seemed to nullify obstruction about the sigmoid flexure. The urine was of high specific gravity (1032), scanty, highly albuminous, but free from sugar. It was found that for some time indication of disease of the kidneys had existed. The occasional cerebral oppression and drowsiness, with cramps in the legs, led us to discuss the question of cancerous disease, but this was laid aside; for, beyond detecting some irregularity of the liver, nothing was found—no jaundice, no previous vomiting, and no growth could be felt before the abdomen became tympanitic. Severe pain and exhaustion preceded death. It was found that there was old disease of the kidneys, one being quite atrophic; there was a constriction of the rectum about seven inches from the outlet; distension of the bowel, but only partial peritonitis; and what was very remarkable, five-sixths of the enlarged liver consisted of scirrhus cancer. It would seem that the exhaustion, which in the one patient led to glycosuria from altered functional activity of the liver, in the other produced cancerous growth. Some years ago a young man was admitted into Guy's Hospital, under my care, with well-marked diabetes. He had previously suffered from a severe burn, but from that he soon recovered. The question was discussed whether there was any causative relation between the injury to the skin and the subsequent diabetes. Dr. Hill has recorded in Dr. Beale's *Archives of Medicine* some interesting instances of glycosuria following burns; and refers to the nervous shock, and the imperfect elimination of carbon and hydrogen by the injured skin, as possible causes of the diabetic state. Whilst referring to the liver in connection with diabetes, we may advert to another indication of change in the functional activity of the gland in that disease. In ordinary diabetes, bile is secreted as usual, and the excreta are well charged with it, whilst the hæmatic relations of the liver are altogether disordered. But at the close of diabetes it is not unfrequently found that a state of complete acholia is induced; the sugar may have entirely ceased, the urine may have become of normal specific gravity, but the excreta are white, diarrhoea supervenes, and sometimes frothy and fermenting evacuations are discharged.

One word in reference to the state of the brain and nervous system in determining to cancerous disease of the liver. When, after severe mental strain or shock, especially of a depressing kind, general impairment of nutrition follows, cancerous cachexia is soon induced. It is in the antecedent condition of cancer that treatment is most available; if we can remove the causes of distress, and procure rest and change of scene; or if indigestion exist, we can mitigate it by remedies, we may avert the full development of a cancerous cachexia; for, when once produced, a very slight excitement will determine its local manifestation, and the presence of gall-stone or direct disturbance of the gland may fix the mischief in the liver, just as a blow may determine the growth of cancer in the breast. When once a growth exists, the time for effective treatment is passed; and when a dyspeptic patient between fifty-five and sixty-five years of age becomes wasted and exhausted under mental strain, there is always danger of cancerous disease, and especially in the liver.

We have already spoken of the ganglion of the vena cava, and its union both with the pneumogastric and with the semilunar ganglion; and it is in this direction that we must look for the explanation of some attacks of severe pain which come on in the upper part of the abdomen during chronic disease of the heart. When from organic disease of the aortic or mitral valve, or from dilatation of the left ventricle or other cause, the right ventricle is distended, the inferior vena cava also becomes necessarily dilated, the liver is congested, the whole portal system engorged, the minute capillary vessels of the mucous membrane are congested, and its altered state leads to the production of thick mucus on the surface of the membrane. In this state, abdominal pain is produced, different in kind, and arising from at least three different causes.

First, it may be a sensation of fulness and throbbing, and of distress at the scrobiculus cordis, which is due to distension of the right side of the heart. This state is relieved by mercurials with squill and digitalis; by purgatives and by diuretics; and, in fact, by any of those means which lessen the vascular strain on the right side of the heart.

Secondly, the pain may be situated across the epigastric region, and is due to the gastric catarrh; the food is imperfectly digested, and becomes coated with a thick envelope of mucus; and flatulent distension is the result. The pain thus produced is often most distressing to the patient; the distension of the stomach impedes the action of the diaphragm and embarrasses to a greater degree the crippled heart. Hæmorrhagic erosion may also be induced, and coffee-ground vomit. This symptom—pain—is lessened by the remedies already indicated, and also by the use of mineral acids, by nux vomica, by carbolic acid, etc., the diet being meanwhile carefully regulated.

A third kind of pain is evidently of a neuralgic character; it is not angina pectoris, but it is abdominal; and I have noticed its locality as situated deeply behind the first part of the duodenum—severe, almost like gall-stone, but without jaundice or its other symptoms; it is not connected with the stomach, for it is not affected by food, but paroxysmal, and recurring sometimes with great regularity. The remedies we have mentioned may be used to their full extent: mercury even to the verge of salivation, digitalis till it can no longer be borne, purgatives may be used freely, and the anasarca removed by puncturing the legs; but still this severe neurosis continues; it appears to be due to exhausted nerve-function, and of those nerves of which we have already spoken. Narcotics and anodynes afford the only means we possess of palliating this distressing symptom.

There are some severe forms of neurosis in connection with the liver and stomach which are difficult of explanation, and which are often very incorrectly referred to gall-stone or to gout. It is perfectly true that spasmodic contraction and severe pain are induced at the pylorus by inflammatory congestion of the mucous membrane, following excesses and intemperance; so, also, in connection with ulceration and cancerous disease of these parts; but the pain indicated is not of that kind, and *post mortem* examination does not reveal these diseases.

Again, intense pain in the region of the gall-bladder and ducts is sometimes due to gall-stone not extending as far as the hepatic duct, and therefore not producing jaundice; or the calculus, as we have known, might be so angular that bile could pass beside it; but the cases to which we refer have presented no gall-stones.

Again, there is no indication of gout in the history or in the general symptoms, no disease of the spine; and we are driven to neuralgia as a name to conceal our ignorance. In an instance of this kind in a man of middle life, who had spent many years at sea as a captain in the merchant service, the periodical attacks of severe pain were so intense, with scanty mucous vomit, that I fully expected to find gall-stones or ulceration in the duodenum. He had remained for several weeks perfectly free from pain or distress, when a fresh sudden attack prostrated his strength; these paroxysms recurred, and in one of greater severity he sank. There were no gall-stones; no ulceration of the stomach or intestine; no abnormal adhesions; no contraction of the pylorus; no morbid appearance, except hour-glass contraction of the stomach, and that we could scarcely regard as the direct cause of death.

I might relate another instance which came under my own notice, which was shrouded in obscurity both during life and equally so afterwards, and in which we were led to attribute the pain to some unknown disturbance of the gastro-hepatic system of nerves. Some of these instances are relieved by nerve tonics, as by arsenic and by steel.

The connection of the pneumogastric with the gastro-hepatic nerves is an interesting one in the pathological study of phthisis; the atrophic deposition of oil-globules in the liver during phthisis is variously explained. A large quantity of carbo-hydrogen may exist in the blood from its undue absorption, and from the imperfect action of the respiratory organs; but a fatty liver is found in other exhausting diseases—in atrophy from intemperance, and from cancerous and other diseases; but we cannot but think that the exhausted nervous energy tends to increase the disease, if so it may be termed. We, however, referred more especially to the indigestion which often precedes phthisis, and which is indicated by pallor, by failing appetite, and by diminished strength; the tongue is furred; and, as it has been remarked by Mr. J. Hutchinson, there is often the dislike to fatty articles of diet. This is the most important time for treatment, before the physical signs of disease are manifested; and that treatment consists less in the administration of drugs than in improving the nutrition of the patient by fresh bracing air, and cheerful healthy occupation. But, at the later stages of phthisis, we sometimes find that the pulmonary symptoms become quiet, the cough nearly ceases; there may be no pain, no diarrhoea, but a complete loss of appetite, a gradual dying out; and although bile is secreted, it is

lessened in quantity, and sometimes it even stops; but it is especially the vaso-motor nerves of the digestive apparatus which seem to have lost their energy and their power to work.

There is a condition of fatty atrophy, or degeneration of the liver, of which we are doubtful whether it is due in greater measure to the condition of the nervous or to that of the vascular system; whether the supply of nerves to the tissues, or the blood, is most at fault. I refer to poisoning by phosphorus; for it is most remarkable that, in a very short space of time, a few hours or days, not only is jaundice produced, but the liver-cells become loaded with oil-globules.

Again, whether the disturbance of the liver in agues and in fevers be due to the nervous system or to the altered character of the blood, there is no doubt that the secretion is changed, and jaundice is produced. Such forms of jaundice are referred to altered enervation of the gland. It is, however, in some of the chronic forms of marsh-poisoning, and jungle-remittents, when no jaundice may exist, that we find the nervous system suffer from extreme depression, and the mental energies seem to fail altogether. There is not the sudden exhaustion and febrile disturbance of the acute attack, but the nervous system lacks its power, and the patient becomes unequal to mental or physical effort. In no class of cases does the value of right treatment manifest itself in a greater degree. Arsenic and bark, with or without the iodides and bromides, soon effect great benefit, and relieve the symptoms of depression.

There are conditions of atrophy of the liver which are due to mechanical causes, such as pressure upon the gland, whether partial, as from compression of the ribs by belt or stays, or from more general pressure of fluid; or again, from interference with the supply of blood, as when a large branch of the portal vein becomes obstructed, and the whole lobe wastes; or from the more diffused obstruction which we find in cirrhosis. These are, however, very diverse from forms of atrophy which are due to the nervous system, and to which some allusion has been made.

The function of the liver is a double one; it has a relation to the blood on the one hand, and to the bile on the other, and in some of the conditions to which we have already referred, the function of the liver is altered in an important manner, but still the secretion of bile is maintained. There is no jaundice, but we have evidence either in the formation of sugar, or by other indications that the gland is functionally disturbed. It is in these instances that the treatment must often be directed to the nervous system; by improving the general health, or by removal to a purer atmosphere; and, if medicines be used, those are most likely to be of service which act upon the nervous system, such as arsenic, nux vomica, nitro-muriatic acid, etc. In a second class of liver disturbance, the hæmatinic relation is affected as well as the secretion of bile, but in a transient manner. The urine contains an excess of colouring matter, of bile-elements, or rather of uro-hæmatine.

We find an evidence of this in the ordinary "bilious attack," and we may ask what is the true pathology of this state? It is sometimes spoken of as stomach-disturbance, and it is in the stomach that the mischief commences. The patient experiences a sense of faintness and exhaustion, it may be of pain at the stomach, vomiting, headache, furred tongue, loaded urine. In a short time these symptoms subside, and health is restored; but how is this condition produced? The irritation of the mucous membrane of the stomach by excess induces weakness or paralysis of the vaso-motor nerve of the liver; there is more blood contained in the gland, the secretion of bile is interfered with, the countenance becomes sallow, the urine altered and thick; at the same time there are often pallor and faintness, for the vaso-motor nerve of the heart is acted upon. Again, the tongue is furred, not, we believe, from direct extension of mischief from the stomach to the tongue, but from the epithelial growth being interfered with by the state of the nervous supply and its intimate connection with other nerves of the same system. The faintness is due to a like cause, and will subside as the irritation lessens. It is unfortunate that this sense of exhaustion and faintness is relieved by stimulants which, for a short time, rouse the exhausted vaso-motor nerve; but the exhaustion as quickly returns, to be relieved by the same remedy. It is most difficult to persuade the patient that the exhaustion is really increased and perpetuated by his stimulant, and that if he will withhold his irritating draught the nerve-power will recover, the appetite return, and the functions will be restored. It may be that in the ordinary bilious attack something may be due to direct absorption by the branches of the vena portæ, and thus direct irritation of the liver may be produced. But this absorption is very slow, and we believe that the symptoms arise principally from the nerve-supply; just as in poisoning by arsenic we have the same exhausted vaso-motor nerve, the faintness, compressible pulse, and loss of power.

In another state, the action of the liver is more profoundly affected; its functional activity is arrested, bile is not secreted, and a most serious

and generally fatal train of symptoms is produced. We refer to *acute yellow atrophy of the liver*. The whole nervous system is arrested in its action, and generally from some intense mental emotion. The patients are nearly always young. Thus, of cases which have presented themselves at Guy's during the last few years, were—

Ellen L., aged 23, who suffered mental distress a few months after marriage.

Elizabeth B., aged 30; no history of mental distress.

William B., aged 25; no history of mental distress.

Frances A., aged 23, a married woman, who had syphilis.

Isabella R., aged 21, a young woman of good family, who had left her home, and had been living as a prostitute.

John C., aged 18.

John S., aged 35, in whom the disease was partial, and in whom there was neither febrile excitement nor delirium.

It will be seen that the greater proportion of these cases is in young women; and in some, pregnancy seems to be connected with the causation of the disease, or rather some intense mental emotion consequent upon that state. The patient is seized with vomiting and headache, and in a short time jaundice follows with cerebral excitement. The temperature is not increased; the pulse is generally quickened; the tongue is furred; there are abdominal pain, nausea, and constipation; the dullness of the liver is diminished, or at any rate not increased; the urine is remarkably changed, and contains two abnormal products—leucine and tyrosine—with diminution of urea, and, according to Frerichs, of phosphate of lime also. The patient sinks from exhaustion generally in the first week. Frerichs states that of thirty-one cases 13 died in the first week; 6 in the second week; 5 in the third week; and 4 in the fourth week. These cases have been recorded by Bright, by Graves, by Budd, Frerichs, Murchison, Harley, etc.; and the anatomical changes in the liver are as remarkable as the physical signs. The liver is lessened in size, the secretion of bile is checked, the gland assumes a deep yellow colour, and, when the affected parts are examined by the microscope, the *débris* of cells only are found; in one instance, I could not find a trace of hepatic cells in any portion of the liver. Nothing could more strikingly show the profound manner in which the gland is affected, but the presence in the urine of such remarkable products as leucine and tyrosine testify to the same fact. In glycosuria we have the formation of products closely allied to other normal constituents, glycocoll, etc.; in ordinary bilious disturbance, the presence of uro-hæmatine in excess shows also that the blood relation function is changed; but in acute yellow atrophy, we have, to use the expression of the late Professor Miller—the elements of putrefactive change; for these abnormal products that have been mentioned may be produced from albuminoid substance by fusing with caustic alkali; ammonia is evolved, and an offensive faecal odour is emitted. Leucine is an unctuous substance, but tyrosine is easily obtained in long fibrous crystals, sparingly soluble in water. This disease is nearly always fatal, and its whole history testifies to its close connection with the nervous system. We believe that successful treatment must be in the same direction; the administration of mercury is probably as likely to be successful as when given in severe septicæmia.

There are, however, instances of the disease in a partial form, and these probably in some cases recover; we have thought that the partial fatty degeneration may have been due to some such cause. In the diagnosis, there is some danger lest we confound with acute yellow atrophy the jaundice which comes on with typhus, or with enteric fever, with ague, or the epidemic jaundice which occasionally occurs, as at Rotherham a few years ago, and which closely resembles a milder form of yellow fever. There is a severe form of jaundice which accrues after irritation of the duodenum and inflammatory disease of the bile-ducts, but in these leucine and tyrosine are absent from the urine, and the cerebral symptoms are, at any rate in the latter case, less severe. Local inflammatory diseases producing jaundice differ also in a similar manner, but the diagnosis is sometimes attended with considerable difficulty. The narration of several instances which have come under my own care will best illustrate this remarkable and rare disease.

[Dr. Habershon read a well marked case in a young woman, aged 21, who became affected with this disease soon after entering upon a life of prostitution. She died on the twelfth day.]

We have tried to show that the nervous system has a most intimate relation with the morbid processes of the liver, even without the production of jaundice; and we are convinced that the treatment must in these cases consist in the removal of nervous disturbance and exhaustion. In a second class of diseases of the liver, the circulatory system is especially modified in the morbid processes; and in these, mercurial medicines, and others having like effect, are constantly of value. In a third lecture we hope to speak of some diseases of the ducts in which alkalies are often of signal service to the patient.