ETIOLOGY AND TREATMENT OF GALLBLADDER DISEASE

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Since the discovery by Pasteur of the bacterial causes of many diseases and the rise of pathology from the days of Virchow, practically all disease entities have been regarded from these two standpoints, viz., patholgy and infection. The question may be raised whether it is not a mistake to attack the problem of gallbladder diseases with only these two points of view in mind. Instead of believing that the thyroid gland can originate a hyperplasia within itself, it is now known that hyperplasia is imposed upon the thyroid gland by factors from without. It is known also that peptic ulcer arises from influences originating outside itself. We now know that these diseases lie within the domain of pathologic physiology rather than in the field of pathologic morphology or of infection. Pathologic morphology and infection may be due to a primary pathologic physiology, which lays the foundation for their development, and this discussion of diseases of the liver and gallbladder is presented with this thesis in mind.

Any theory which attempts to explain the genesis of gall stones and of gallbladder disease must explain their distribution in nature and the sex and age incidence of the disease. It must account for the fact that gall stones occur more frequently in certain races, that they occur more frequently in women than in men, and further, that they occur more frequently in women who have borne children.

What is the distribution of gall stones in nature? Broadly speaking, this disease is less common among wild animals in captivity than in domestic animals, and the carnivora are more subject to the formation of gall stones than are the herbivora. This was found to be true by Dr. Herbert Fox, Pathologist at the Philadelphia Zoological Gardens, who has reported finding gall stones in but fourteen out of 6000 autopsies performed on wild animals which were in captivity.

Among human beings there is a significant distribution of gall stones and of gall stone disease. It has been observed that the highest incidence of gall stones is found among the Hebrew and Latin races while they are relatively uncommon in the colored race and among the Hindus, the Chinese, the Japanese and the Koreans, as compared with the Europeans and the Americans. Differences in diet among these peoples must, of course, be taken into account, since Walsh has shown that gall stones are more likely to occur in patients who have had a diet low in vitamins, especially in the fat-soluble vitamins A and D. Gallbladder disease is not found so frequently in people of a lower order of civilization or in persons who, though they may

belong to a higher order of civilization, have a negative philosophy of life.

It would seem, therefore, that there are certain factors operative in highly-developed, high-strung, emotional, active persons and in childbearing women that can change the concentration of the bile salts secreted by the liver cells, this concentration being due to a change in the activity of the cells of the liver. Ivy and Walsh and others have shown by their experimental work in dogs and by experiments in vitro that the outstanding factors that govern the maintenance of the cholesterol and pigment in solution in the bile are the bile salts and the fatty acids. It is readily seen that when gall stones or infection interfere with the free flow of bile in and out of the gallbladder, there results an immediate interference with the concentration of the bile salts and fatty acids and further formation of gall stones is promoted by the diminished concentration of the solvent bile salts. Thus, an infection, by interfering with the concentration of the bile, would probably promote the formation of gall stones. But the question is raised whether the infection is not the *result* rather than the *cause* of gall stones.

That this is the case is attested by the fact that it has been estimated that there are now in the United States twelve million people who have gall stones and do not know of their presence. Moreover, relatively few patients have an infected gallbladder or an abscess in the gallbladder without stones. Infection does not play the primary rôle in causing the depression of the function of the liver cells but rather depression of the function of liver cells occurs as the result of a general infection, acute or chronic, emotional excitation, pregnancy and excessive eating. Each of these conditions has the power of changing the concentration of the bile salts and in consequence promotes the formation of gall stones. Therefore, it is not infection, but altered function of the organism, which furnishes favorable conditions for the formation of gall stones, and those men and women whose livers are more often subjected to that kind of change, which will alter the concentration of the bile and the amount of the fatty acids, are the men and women in whom there is a high incidence of gall stones.

The key to the explanation of the above picture was provided by certain histological and biophysical researches instituted twenty-five years ago which have provided the explanation of certain facts regarding the incidence and behavior of gall stones.

A histologic examination was made of every organ and tissue in animals that had been subjected to insomnia, fear, physical injury, shock, prolonged anesthesia and infection. In every case histologic changes were observed in three organs and in three organs only—

the brain, the liver and the adrenal glands. In the liver the cells lost their differential stainability—they became swollen and misplaced, the cytoplasm was vacuolated, the nuclei were crenated and the cell membranes were irregular. The most marked changes occurred in the cells nearest the periphery of the lobules. Later, identical changes were found in the liver cells of patients who had died from infection, from hyperthyroidism, or in any case in which exhaustion was due to the protraction or intensity of the disease. Later biophysical researches disclosed that, under the same conditions, changes took place in the temperature and in the electric conductivity, electric capacity and electric potential of the liver.

Hyperkineticism presupposes primarily to hyperactivity of the adrenal-sympathetic system. Pregnancy, infection, emotion, foreign proteins—all hyperkinetic conditions—produce an immediate change in the cells of the liver. Change in the cells of the liver in turn presupposes a change in the bile content; change in the bile content, as shown by experimental research, leads to the formation of gall stones.

It has been established by laboratory experimentation that the liver performs its function in part through direct nerve stimulation over the sympathetic system and in part through hormone action; and that for the performance of at least part of its function it must have a simultaneous hormone and nerve stimulation. The nerve supply of the liver is derived from the sympathetic and parasympathetic system, the nerve fibres passing along the blood vessels and the common duct. In addition to the nerve supply to the liver as a whole, each separate liver cell has its own nerve supply, not only on its outer border, but a filament of nerve tissue penetrates each separate cell.

One would expect to find that an organ, every unit of whose structure is thus wired, would have a close relationship with the great functions of the body. This rich sympathetic supply of the liver is of special importance as it supplies a connection between the adrenal glands and the liver. Experimental researches have shown that when the adrenals were removed, the liver cells undergo disintegration; while after decapitation, if the adrenals remain intact, the liver cells do not break down. Moreover, the injection of adrenaline increases the stainability of the liver cells followed by loss of stainability. To the extent, therefore, that the sympathetic innervation of the liver is interfered with, to that extent is the adrenal influence removed from the liver, and the diminished influence of the adrenals will be registered in the liver cells.

There is nothing more definitely established than that the injection of adrenline, the expression of an emotion, the presence of a foreign

protein or of an infection, or a great exertion, or a physical injury produces an increased activity of the energy system of the organism, and the liver is linked indissolubly with that energy system. All the factors that cause an increased output of adrenaline in the experimental laboratory have the power of changing, of modifying, of interfering with the cells of the liver, and, in consequence, with their production of bile.

Physical injury and anesthesia also produce changes in the liver cells, and this fact has a direct bearing upon the operative treatment of gallbladder disease, for it follows that the management of the patient should be directed primarily to the restoration of the already impaired liver cells and the protection of those cells from further damage.

The question then arises as to what treatment should be instituted for these highly-developed, high-strung, emotional, active persons and childbearing women whose liver cells have undergone changes which result in alteration in the concentration of the bile salts and formation of gall stones.

The surgical procedure to be preferred is cholecystectomy, unless the condition of the patient is such as to render this operation inadvisable, in which case conservative measures must be resorted to as the only alternative.

Anesthesia: Experimental researches have shown that physical trauma and inhalation anesthesia affect the liver cells. Therefore it is obvious that for the protection of liver function, minimum trauma must be inflicted and that the anesthesia must not be carried beyond the minimum degree necessary to secure the required relaxation. This is obtained in most cases by local, regional and splanchnic anesthesia with nitrous oxid analgesia. In obese patients, spinal anesthesia is preferred but it should never be employed in the presence of an associated high blood pressure or of nephritis. As an added precaution against the effects of the lowered blood pressure due to spinal anesthesia, a blood transfusion may be given just before the anesthetic is administered.

Our researches have shown also that every exhaustion-producing stimulus—anesthesia, physical injury, emotion, etc., reduces the temperature of the liver. Therefore, both the liver and the brain must be protected to the utmost against further cooling by the exposure of the viscera. To avoid such a condition which formerly was termed "liver shock", the surgeon must be prepared to execute every maneuver with the constant objective of protecting the liver against operative trauma, against interference with its nerve supply and against cooling of the intra-abdominal organs. In cases in which

the hepatic function is low, it is best to defer operation and to administer a high carbohydrate diet and glucose solution intravenously until the liver shows evidence of restoration of its normal function.

Operative technic: The following points are essential in the technic of cholecystectomy: (1) The gall bladder must not be opened. (2) The liver tissue must not be injured or laid bare. (3) The cystic duct and the cystic duct alone should receive the ligature. (4) The common duct must not even be crowded by the ligature. (5) Not even a fragment of the base of the gallbladder should be left. (6) The field should constantly be kept so clear that an accessory or abnormal duct can be seen. (7) In general, the duct and the artery should be tied separately, although if the common pedicle is small, there would seem to be no risk in tying them together. (8) To prevent adhesions, to minimize oozing, to control the transudation of capillary bile, the raw surface of the liver, if any, should be closed by means of a fine, round, curved needle, the stump being buried beneath the suture line. Closure of the cystic duct with broad bladed, curved forceps is a most important step in the removal of the gallbladder so that no stones may be pushed into the common duct.

Drainage: Many, perhaps most, clean cholecystectomy wounds theoretically can be closed without drainage, yet occasionally there will be an unusual case, in which bile leaks in some unexplained way and bile peritonitis threatens or may even cause the death of the patient. The probable explanation is that some small aberrant bile duct, through which a small hepatic area is drained directly into the gallbladder, is unknowingly divided, so that after the wound is closed it oozes unnoticed until bile peritonitis is established. This occasional occurrence supplies the argument in favor of drainage in every case. This argument is the more convincing because bile peritonitis is one of the most difficult complications to recognize. The patient may appear very well for several days, and then suddenly, probably because of the gradual increase in the quantity of bile which has escaped, may become desperately ill.

Prevention of Postoperative Complications: Gallbladder infection and gall stones cause pain and indigestion as the result of the disturbance of the delicately balanced autonomic nervous system. If, in the removal of the gallbladder, the sympathetic nerves, which are almost devoid of shielding coats, are disturbed or injured or laid bare, postoperative digestive disturbances will occur, adhesions will form, and there will be a long course of pain and indigestion resembling the symptoms before the operation. It is not surprising

that there should be postoperative symptoms that are so similar to the pain and indigestion which accompany cholecystitis, since both before and after operation, the symptoms are caused by disturbance of the sympathetic and parasympathetic nerves.

A proof of the validity of this point of view is the fact, that to the extent that the autonomic nervous system is protected against postoperative scar, to that extent will postoperative pain and indigestion be diminished. Since the technic has been conducted scrupulously to avoid disturbing the sympathetic system, and the practice of a splanchnic block by injection of novocain through the posterior peritoneum in the region of the sympathetic complex has been instituted, painful indigestion, gas, etc., have been prevented in the later clinical course.

Summary and Conclusions

The highest incidence of gall stones is found among hyperkinetic and emotional persons. There is a higher incidence among women than among men and this is higher in women who have borne children. This is accounted for by the fact that those persons who are affected by the disease are those who are highly-developed, high-strung, emotional, active persons or pregnant women whose energy system has been subjected to increased activity. These factors change or modify the concentration of the bile salts secreted by the liver cells. Therefore, pathologic physiology rather than pathologic morphology and infection is responsible for the formation of gall stones.

The treatment of preference is cholecystectomy except in those cases in which this operation is inadvisable. The preoperative, operative and postoperative phases of the treatment must blend together so that they do not counteract each other. The establishment of chemical and nervous equilibrium by preoperative measures is extremely important and physical and mental rest and the re-establishment of the electrolytic and glucose balance contribute to the desired end. During the operation the depression of the protoplasm by the anesthetic, by a fall in blood pressure, by shock, by lowering of temperature, must be reduced to the absolute minimum. Sharp dissection and care in handling the sensitive tissues are imperative. When these general measures are employed, the immediate as well as the later course of patients subjected to oprations on the gall-bladder and ducts is relatively smooth.