ART. XIV.—*Observations on Jaundice; and Hemorrhage in Affections of the Liver.* By CATHCART LEES, Physician to the Meath Hospital; Lecturer on Practice of Medicine.

MANY cases of jaundice have occurred in which delirium, convulsions, and coma supervened, and proved rapidly fatal, although accurate examination failed to discover any mechanical obstacle to the passage of bile out of the system, the bile ducts being pervious and empty; so that this form of disease has been described as fatal jaundice from *suppressed secretion* of bile, which means, that the jaundice in such cases depends on the retention in the blood of the elements of the bile, which in the healthy state is separated only, not formed at the liver, and which, when retained, acts on the nervous system nearly as a narcotic poison,—causing a condition of the system analogous to that occasioned by the suspension of the secretion of urine in cases of ischuria renalis, or in some cases of albuminuria. Dr. Alison explains this by supposing that “the retention in the blood of matter destined to excretion is much more hurtful to the living body than the *reabsorption* into the blood of matters which have been excreted at their appropriate organs, but not discharged from the system in their natural way, owing to some mechanical obstruction in either the biliary or urinary passages.” In reference to this class of cases, Dr. Budd, in his work on Diseases of the Liver, after detailing some observations recorded by Alison, Bright, Graves, and others, thus writes: “It does not seem possible to deduce from the cases that have been related any sure means of distinguishing jaundice that results from suppressed secretion, from jaundice produced by temporary closure of the ducts, except in the particular cases where the jaundice immediately follows a powerful emotion, or occurs in the course of purulent phlebitis; or in consequence of known poisoning; or where, as in the instances related by Dr. Griffin and Dr. Hanlon, it occurs with peculiar characters in several members of a family, or in several persons living together, in succession. In all these instances knowledge of the cause of the disease, or of some peculiar circumstances under which it may have arisen, gives significance to symptoms that would otherwise be vague and ambiguous. In other instances, where our judgment must be formed from the symptoms merely, the diagnosis is much more difficult.” Now, it has struck me that the examination of the urine might be of some use in

forming not only our diagnosis, but also our prognosis in these cases of jaundice, particularly as in none of the cases recorded by the writers I have mentioned is there any analysis given of this secretion. I have, therefore, had the urine in some cases of jaundice carefully examined by competent persons lately, and shall proceed to detail one case, and give the results of two others nearly similar, in all of which an important principle of the bile was detected in the urine.

CASE I.—*Jaundice from Retention of Bile; Cholic Acid in the Urine*^a.

Michael Holloned, aged 48, was admitted into the Meath Hospital January 15, 1854. For two years previous to his admission he had been subject to occasional attacks of dyspepsia, which not being severe, and causing but little inconvenience, did not excite attention. In July last he first experienced slight difficulty in swallowing, which he ascribed to some obstruction to the passage of food existing in the situation of the xiphoid cartilage. The dysphagia, which was always more severe after taking solid food, was after some time followed by vomiting soon after eating, and which presented a dark brownish appearance. About this time he also complained of severe gnawing pains, at first occupying the epigastrium, but afterwards extending to the right hypochondriac region. These symptoms increased in severity. The vomiting, which was occasional at first, now became constant, and the matter assumed a whitish, slimy appearance. He was greatly emaciated, and a few days previous to admission became jaundiced. His habits in early life had been very intemperate; none of his family, to his knowledge, had been afflicted with any malignant disease.

On examination, after admission, slight hepatic enlargement was detected. There was no irregularity of the integuments, nor could any tumour be observed over the surface of the abdomen. The superficial abdominal veins on the right side were slightly enlarged. The thoracic viscera seemed healthy, with feeble respiration over the right lung.

The jaundice was general, and of a dark green tint. The bowels were obstinately constipated, and the fæces presented a whitish appearance. The urine was of a dark-brown colour, containing bile, and coagulating on exposure to heat. The

^a Reported by Mr. Andrew Nolan.

vomiting and dyspeptic symptoms were considerably relieved by the exhibition of bicarbonate of soda in combination with hydrocyanic acid, but the patient gradually lost flesh, and was attacked with severe pains in his bones, increased on the slightest exposure to cold, so that he could not even bear the clothes to be removed for the purpose of examination. He now suffered from constant vomiting, the stomach being so irritable that nothing but cold tea would remain on it; he gradually sank, and died in a state of syncope, not having had any delirium, convulsions, or coma, his intellect remaining clear up to his death. On examination, the liver was found to be slightly enlarged, of a deep olive colour, its convex surface smooth, but there were some small cancerous deposits in the left lobe; on its under surface there was a large amount of cancerous deposit. The gall-bladder was distended with bile, and the hepatic and common ducts greatly dilated, being pressed on and involved in a large mass of cancerous glands which surrounded them. A large cancerous deposit in the submucous tissue of the stomach surrounded the cardiac orifice, and there was a perforation on the anterior surface of the lesser curvature. The mesenteric glands were in a state of cancerous degeneration. The kidneys and spleen were healthy. On examination of the liver under the microscope hardly any distinct cells were visible; numerous oil globules and irregular particles of yellow and orange biliary matter filled the field, forming a confused mass of amorphous particles.

This case presents many points of interest: first, as to the diagnosis of the cause of the jaundice; I pronounced from the day of his admission that I considered it a case of retention of bile from the presence of cancerous tumours in the liver, making pressure on either the hepatic or the common duct, and thus preventing the passage of bile into the intestine; this cancerous affection of the liver I considered to be secondary to cancer of the cardiac orifice of the stomach, reasoning from the history and progress of the case, as his complaints were first referable to the stomach, then pain extended into the right hypochondriac region, and finally jaundice appeared. I made the diagnosis of cancer of the stomach from the appearance of the patient, and from the microscopical characters of the matter vomited, which Mr. Ledwich examined carefully with me, and in which we detected oil globules, granular cells with included nucleated cells and a few blood globules, but mostly changed in form; for though the patient stated, that what he had occasionally vomited resembled coffee-grounds, yet the matters

vomited while under our observation were not of this character, but appeared to consist of mucus tinged with bile. I may here mention that the colour of what is termed the coffee-ground vomit which is met with in cancer of the stomach, and also of the black vomit which occurs in yellow fever, and in some cases of malignant typhus and other blood diseases in this country, appears to be caused by granules of a dark brown pigment, consisting of the altered colouring matter of the blood, mixed with a number of blood globules mostly altered in form. The enlargement of the liver occurring subsequently to these symptoms, and persisting up to his death, led me to diagnose cancer of that viscus, though, from not being able to detect any irregularity on its convex surface during life, I considered that the disease was seated in the under surface, where it would be most likely to implicate the bile ducts, and the dark green colour of the jaundice confirmed me in this opinion, which the post-mortem examination proved to be correct. I certainly was not prepared to find perforation of the stomach, as he did not present any symptoms during life of that lesion; and as there were no traces of peritonitis, I presume that the perforation must have taken place a very short time previous to his death; besides, from its position being situated in the anterior surface of the stomach, there was no effusion of the contents into the peritoneal cavity, and consequently no inflammation existed. The chief points in this case, however, to which I wish particularly to direct observation are, first, the perfect immunity which the nervous system appears to have enjoyed up to his last moments, as he had neither delirium, convulsions, nor coma, though the system was deeply saturated with at least the colouring principles of bile; and second, the condition of the urine. This secretion was carefully examined by Mr. Leet^a, one of our most intelligent pupils, who furnished me with the following account of his analysis:—

“The urine excreted early in the morning had a dirty brown colour, a peculiar odour, like putrid fish, and formed some hours after emission a scanty deposit, which on being submitted to the microscope presented a few grayish, round vesicles, which disappeared on the addition of ether; some renal and tessellated epithelium, deeply coloured with bile, and some dark granules of irregular form, which dissolved in a solution of potash, (pigment cells). Its reaction to test-paper was

^a This gentleman obtained the first prize in chemistry given by the Apothecaries' Hall of Ireland.

strongly acid, and its specific gravity 1·013; 1000 parts yielded on analysis the following:—

Water,	969·8
Solid constituents,	30·2
Urea,	8·6
Uric acid,	0·9
Coagulum ^a ,	7·8
Biliary matter ^b ,	5·7
Fixed salts,	3·2
Alkaline salts,	2·5
Earthy phosphates,	0·7
Organic matter and ammonia salts,	4·0

The result of this analysis led me to entertain the opinion that the absence of any symptoms referable to the nervous system in many cases of jaundice might be accounted for by the presence of cholic acid in the urine, and its consequent absence from the blood. I was confirmed in this suspicion by the examination of the urine in two other cases of jaundice from retention of bile, recently under my care, and in which Dr. Simpson, Lecturer on Chemistry in the Original School of Medicine, Peter-street, arrived at similar conclusions with regard to the presence of this principle of the bile in the urinary secretion, while there was the same immunity from any affection of the nervous system, though post-mortem examination proved that

^a This substance coagulated from the urine at the boiling point in yellowish-white amorphous flakes, insoluble in water, ether, and alcohol, but readily dissolved by hydrochloric and concentrated acetic acids, giving in these solutions copious yellow precipitates with ferrocyanide of potassium; it was also precipitated from the urine by dilute acetic and phosphoric acids as well as by ether; but no change took place on the addition of nitric acid, solution of bichloride of mercury, or strong alcohol. Again, when heated in the coagulated form with concentrated nitric acid, it produced a deep yellow colour, and with concentrated sulphuric acid an intense blue; the insoluble modification also entirely dissolved in solutions of potash and soda, being again precipitated on neutralization with acids. From these characters it is clear that this coagulum was not albumen, though closely resembling it, but was, in all probability, one of the same class, that is, a protein compound.

^b This substance was obtained by evaporating a portion of the urine, precipitating the water extract and the salts insoluble in alcohol, with spirit of 0·85; evaporating again this solution, and extracting the residue with anhydrous alcohol, and having expelled the spirit of this solution, the residue was dissolved in a little water, and some hydrochloric acid added, and allowed to digest till this substance had separated itself. It had a resinous appearance, a greenish-brown colour, was almost insoluble in water, but entirely dissolved in alcohol, which solution was distinctly acid, and produced an intense violet red colour with solution of sugar and sulphuric acid when applied in the manner proposed by Pettenkofer; on the addition of nitric acid also it formed a faint pinkish-red colour. From these reactions and others which need not be alluded to, it may be safely inferred that this biliary matter was chiefly composed of the peculiar organic acid of the bile—cholic acid, and a small proportion of its colouring matter—or bile pigment.

complete obstruction to the passage of bile from the liver existed. Now, if this supposition be correct, I think that the detection of cholic acid, or its conjugates in the urine, may prove a very important element of prognosis in every case of jaundice, as assuring us against the supervention of cerebral symptoms in cases where it is present, while, if absent, it may put us on our guard, and possibly enable us to adopt a prophylactic treatment. Its presence or absence might also help to explain some of those apparently anomalous cases in which the liver has presented every appearance of the "acute yellow atrophy," so well described by Rokitansky, and yet no cerebral symptoms had preceded the death of the patient; though as a general rule the union of jaundice with cerebral phenomena is mostly found connected with this peculiar condition of the liver. This subject is also of importance with reference to a statement made by Dr. C. Handfield Jones in "Some Observations on the Effects of Cholagogue Medicines," published in the thirty-fifth volume of the *Medico-Chirurgical Transactions*, in which he states that "the deep colour of the urine in jaundice also seems to depend *solely* on the presence of the pigment; *no trace* of cholic acid is often discoverable. He, therefore, concludes, that "in most cases jaundice results from the absorption into the blood, not of completely formed bile, but of one of its constituents only, viz., the yellow pigment." Professor Lehmann in his *Physiological Chemistry* adopts the theory "that the components of the bile are not formed in the blood," and in support of this opinion adduces the fact, well-known to every practical physician, that jaundice seldom occurs in disease in the parenchyma of the liver: "certainly never in fatty liver, in the lardaceous liver, nor in tuberculosis of the liver, and but seldom in cirrhosis, or in inflammation of its substance;" so that, if bile can still be formed with all these various alterations of the parenchyma of the liver, it is highly probable that some other apparatus beside the cells has a large share in the formation of this secretion, and would thus tend to support the opinion of Dr. C. H. Jones, that "the bile is not completely formed in and by the hepatic cells; but that this is effected by the action of the ultimate ducts:" for he considers "inaction of the elaborating ducts to be a very common cause of jaundice, the cells becoming filled with yellow pigment because it is not withdrawn from them." This condition of the cells would be an argument against the old opinion, that has been recently put prominently forward by Dr. Henoch, of Berlin, in his late work on "*Abdominal Diseases*," in which he maintains that

in all cases jaundice arises from the reabsorption of bile, both by the veins and lymphatics of the liver, as stated by Saunders many years ago. The last point I shall allude to is the fact of the presence in the urine of renal epithelium tinged with bile, and which I think is of interest, as showing that when from any cause the functions of the liver are imperfectly discharged, so that the bile accumulates in the blood, the kidneys make an effort to eliminate some of the constituents of the bile, and thus some of the renal epithelium becomes detached and is washed away by the urine, in its passage through the tubes of the kidney.

The frequent occurrence of *hemorrhages* from the stomach and bowels in cases of cirrhosis of the liver is now so familiar to every practical physician that they may be considered as standing to each other in the relation of cause and effect; and we can explain them in a great measure by the mechanical obstruction given to the portal circulation in the liver; but the great influence which other diseases of the liver exercise on the production of hemorrhage generally, has not received the attention it appears to me to merit. Thus we meet with it in simple congestion of the liver, in inflammation, in cirrhosis, and in malignant disease of this organ, so that the mere fact of its occurrence in a doubtful case is of great assistance in making our diagnosis; as, for instance, where the abdomen is greatly distended with fluid, and we are in doubt whether the effusion be ascites depending on disease of the liver, or whether it be a large unilocular ovarian cyst; if the patient has been subject to hemorrhage from the stomach, bowels, or even from the nose, it furnishes strong evidence in favour of the liver being the organ diseased. Now, though in many of these cases we can explain the rationale of the hemorrhage by mere physical causes, yet in others in which we cannot detect any mechanical obstacle to the circulation in the liver, it is difficult to account for it, except on the supposition of a change in the chemical composition of the blood, which we can easily conceive; as, no sooner is the liver affected in either its functions or its substance, than the depuration of the blood is interfered with; in some cases the colouring principles of the bile are retained in the blood, and then there results jaundice, which may occur rapidly, and be accompanied by very serious and fatal symptoms, as in those cases termed "suppression of bile;" or it may supervene gradually, and not be attended with any important symptom, though, according to the recent researches of Claude Bernard,

the transformation of albumen into fibrine is but imperfectly effected in these cases, and it is supposed that the separation of fatty matters, and of the acids proper to bile, are also interfered with; as to the sugar, it continues to be formed in the liver and destroyed as usual, for we cannot detect it in the urine; so that, without precisely specifying the parts or the functions of the liver which are affected, we may conclude that the blood is not properly elaborated, but contains certain principles of which it ought to be deprived in the liver; and if this state persists for some time there results a tendency to hemorrhage from the stomach and intestines, partly due to the injury done to the capillary circulation of the liver, and partly to a morbid condition of the blood. In the following case of jaundice, hemorrhage occurred from a different source, and as the case presented some interesting points, I think it may be useful to record it.

John Smith, aged 45, a servant, was admitted into the Meath Hospital in March last, with jaundice, of a dark-green hue: he was greatly emaciated, and complained of pain and sensation of distention in the epigastrium; the liver filled up the right hypochondriac region, where it formed a smooth tumour, tender on pressure; the superficial veins of the abdomen were dilated, but there was no ascites nor enlargement of the spleen. The urine was deeply coloured with bile, and contained cholic acid; the *fæces* were devoid of bile. He stated that he had always enjoyed good health until last November, when he first began to suffer from dyspepsia, with pain in the stomach; and about three weeks ago he gradually became jaundiced; since that he has vomited blood on one occasion, and has also passed blood from the bowels; he had no fever, but was very heavy and apathetic; there was some dulness with increase of the normal physical signs at the root of the left lung, but no cough nor expectoration; tongue was clean, but dry and fissured. He was put on palliative treatment of taraxacum and soda, his bowels regulated by mild aperients; but the jaundice gradually increased, and he died quietly without any cerebral symptoms. On examination the liver was smaller and softer than natural, but presented a dark olive colour, evidently saturated with bile; there was one solitary cancerous deposit on its upper surface; the gall-bladder and the ducts were distended with bile. The stomach was enormously dilated, its great curvature extending far below the umbilicus; it was filled with fluid the colour of ink, which also distended the intestines; a large chronic ulcer was seated in the lesser curvature, and had protruded the mucous coat. The mucous

membrane of the centre of the vertical portion of the duodenum was removed by cancerous ulceration for about one inch in extent, and its place supplied by the pancreas, which formed the base of the ulcer. On microscopic examination the parenchyma of the liver appeared to consist of a mass of broken-up granular matter, tinged deeply with bile, and mingled with oil-drops; scarcely a distinct cell was visible, nor could the lobules be distinguished in it.

The chief points of interest in this case are, first, the effect which the closure of the ducts had on the liver itself, evidenced by the enlargement of this viscus at first, and then its subsequent diminution in size, which was explained by the destruction of the proper secreting cells, which, combined with the pressure of the retained secretion, exerting its influence upon the nutrition of the essential elements of the organ, seems to have occasioned atrophy of the capillary vessels subservient to their secretion; and from these conditions there resulted a gradual disappearance of the secreting cells, and atrophy of the substance of the liver, analogous to the atrophy of the kidney from obstruction of the ureter, so that the cessation of the process of secretion, and the wasting of the capillary vessels, probably render the passage of the blood through the liver less free in these cases, and thus tend to explain the occurrence of hemorrhage. In this case, however, I think the hemorrhage came from the chronic ulcer of the stomach, and the peculiar inky fluid which we found in it was decomposed blood. The great emaciation in this case may be explained by the inclusion of the pancreatic duct, which was confounded in the cancerous mass with the common duct. There is also another point worthy of notice: we found the anterior lobes of the lungs very emphysematous, completely covering the heart, so that it appeared as if pushed backwards by the distended lung, which might account for the dull sound on percussion heard at the root of the left lung, and which I at first supposed might have been due to cancerous deposit in this organ.

I have not alluded to apoplexy of the liver, as it is a distinct form of hemorrhage from the viscus itself: it is a very rare occurrence, and has been well described by Rokitansky in his *Pathological Anatomy*. A very remarkable case of it was recorded by Dr. Foote in the last number of this Journal.