

**Jaundice : its pathology and treatment with the application of physiological chemistry to the detection and treatment of diseases of the liver and pancreas / by George Harley.**

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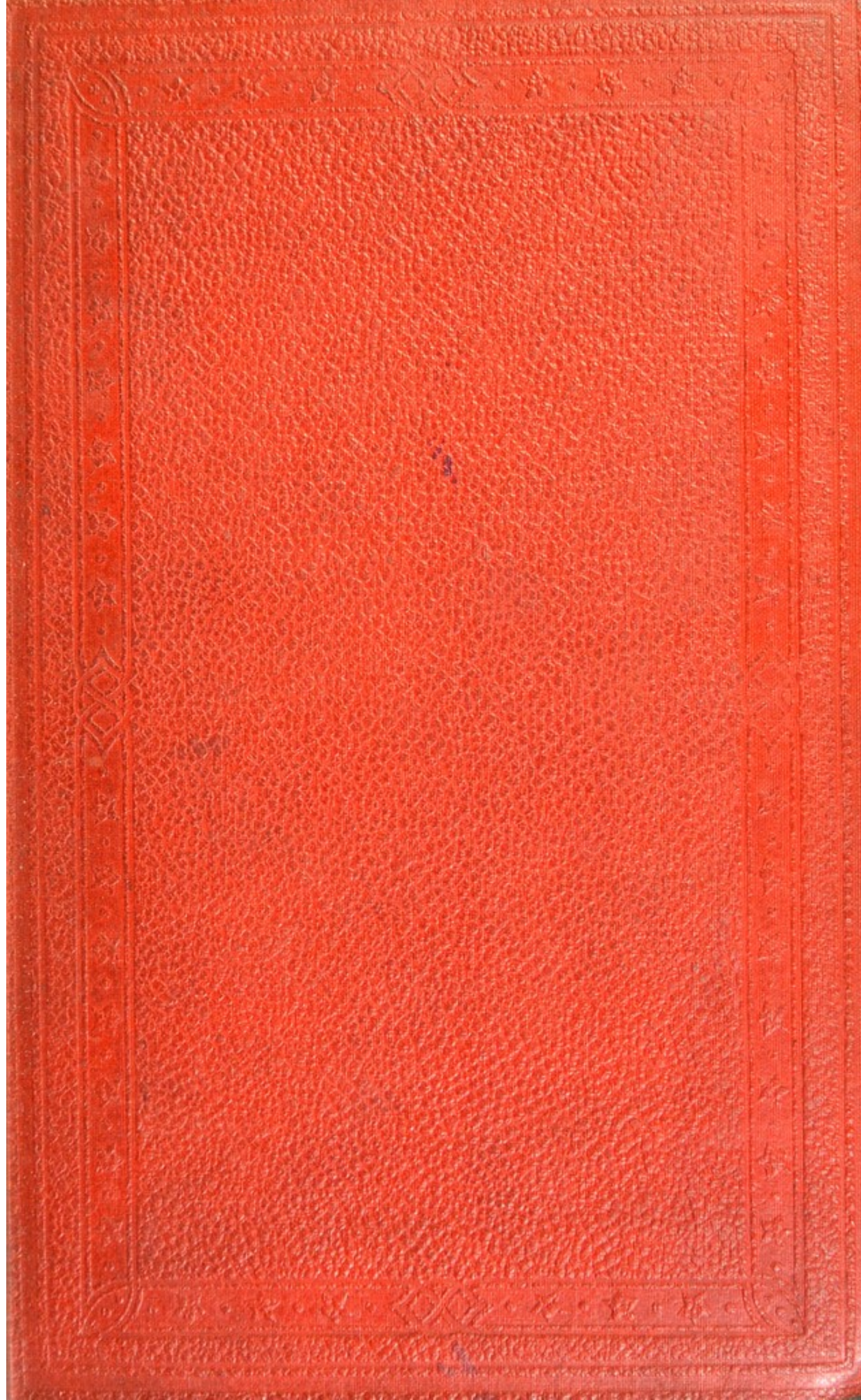
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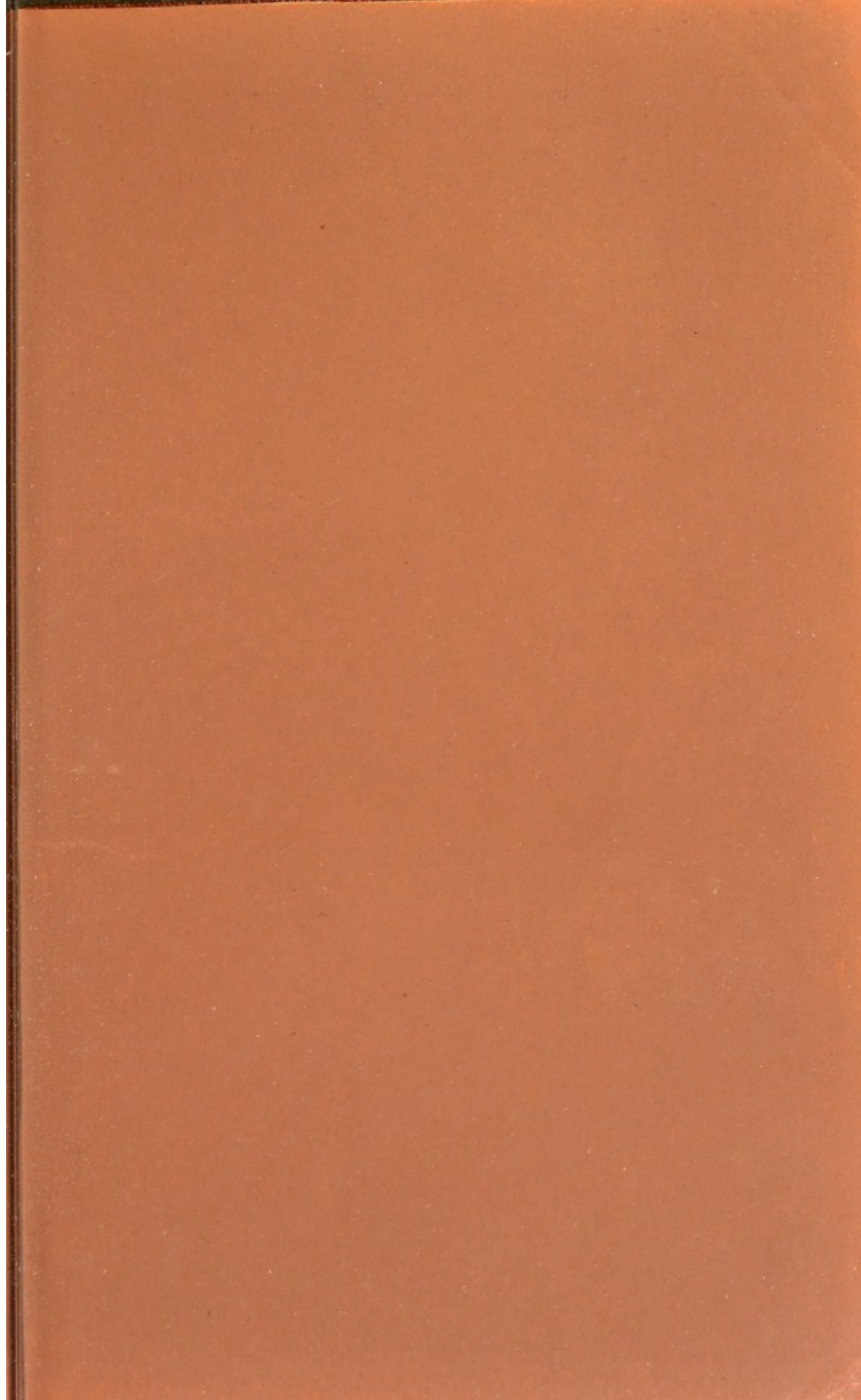






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JAUNDICE:  
ITS  
PATHOLOGY AND TREATMENT.  
WITH THE  
APPLICATION OF PHYSIOLOGICAL CHEMISTRY  
TO THE DETECTION AND TREATMENT OF  
DISEASES OF THE LIVER AND PANCREAS.

BY

GEORGE HARLEY, M.D.,

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So rapid is the advance of science, that the theory regarded as true to-day, may be recognised as false to-morrow. The facts, however, on which the theory is based, if rightly observed, remain unaltered, and unalterable.

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TEMPLE BAR.

TO

WILLIAM SHARPEY, M.D., LL.D., F.R.S.,

Professor of Anatomy and Physiology in University College, London,

AS

A SMALL TOKEN OF A COLLEAGUE'S ESTEEM

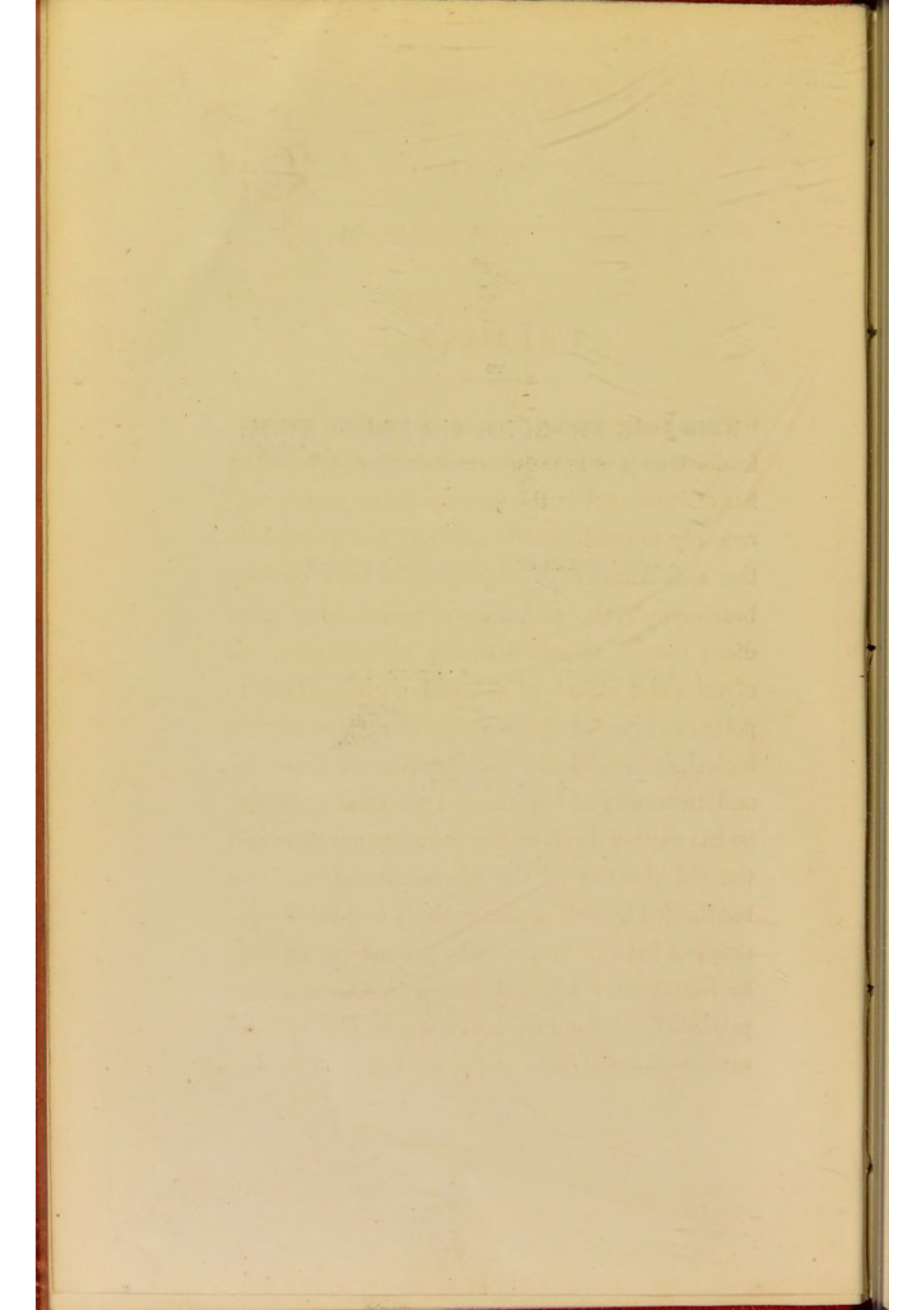
FOR

A PROFOUND THINKER, A SOUND REASONER,

AND

A TRUE FRIEND.





## P R E F A C E.

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"TIME being money," quite as much to the professional as it is to the mercantile man, the author has endeavoured in the accompanying monograph not only to condense his material, but to exclude the consideration of any question not directly bearing upon the pathology or treatment of jaundice; indeed, as stated in the Introduction, one of the chief objects of the author having been to point out how valuable an adjunct modern physiological, and chemical knowledge is in the diagnosis, and treatment of hepatic and pancreatic disease, he has neither dwelt on the literature nor discussed the old theories of the mechanism of jaundice, but limited himself almost entirely to a brief exposition of his own views. For the sake of brevity, he has at page 132 put into a tabular form the pathology of jaundice, according to the opinions expressed in the body of the volume.



As the object of all theory, and the aim of all science, is to insure wise practice, the author desires to call special attention to that portion of the work devoted to the chemistry of the excretions, feeling, as he does, that we are entering upon the threshold of an important department of medical inquiry, which, sooner or later, will be followed by valuable practical results. He would also direct the special attention of his readers to the chapter devoted to treatment, being sanguine enough to imagine that the adoption of the principles he has enunciated regarding the mode of action, and administration of the remedies usually employed in hepatic affections, may conduce to a more rational and successful method of treatment than has hitherto been employed. He even goes far enough to hope that the result of the treatment, as shown in the cases cited, will not only justify the adoption of the principles on which it is founded, but also prove a strong incentive to others to follow the line of diagnosis he has striven to inculcate.

In some portions of the volume the statements

of the author may, perhaps, appear to be rather dogmatic; if so, he would remind his readers that this has arisen from the circumstance of so many old dogmas, and deeply-rooted prejudices having to be combated, for he is quite alive to the fact, that what we regard as scientific truth is in no case incontrovertible certitude, and that the deductions of to-day, in an advancing science like that of medicine, may require material alteration when viewed in the light of the morrow. But he is equally convinced of the fact, that if men fold their arms, and refrain from acting until every link in the chain of knowledge is forged, all progress will be arrested, and the day of certainty still further postponed.

Too long have we reversed the natural order of things, and commenced the study of medicine where we ought rather to have left it off. Too long have we striven, by studying pathology ere we were sufficiently acquainted with physiology, to place the pyramid on its apex instead of on its base; and thus it is we remained so long ignorant of the fundamental doctrine, that the same laws



which regulate health, regulate disease. Nature does nothing on a small scale, and the more we study her the more we admire the uniformity, and extensive applicability of her laws. If we pry into the ultimate structure of our bones, we find they receive their nutriment by a system of irrigation, carried on through lakes, and rivers (*lacunæ*, and *canaliculi*); and if we examine the periosteum surrounding them, the ligaments attaching them, or the muscles covering them, we still find, that, notwithstanding the diversity in structure, and use, the one system of irrigation pervades them all. We may even go a step further, and say that the same law which governs the animal governs also the vegetable kingdom. Indeed, the further science advances, the more apparent does it become, that not only the animal, and vegetable, but even the organic, and inorganic, form but one world, regulated by the same laws.

A knowledge of organization, important though it be, is yet less indispensable to the physician than a knowledge of healthy function, for it is

the latter which elucidates the dark problems of life, it is the latter which proves the golden key to the comprehension of disease.

Although not even the most ardent admirers of medicine can say, that it as yet merits the name of an exact science, this ought neither to destroy our hopes nor trammel our labours. With the stethoscope, microscope, and other physical means of diagnosis a new era dawned upon our art; and now the members of the new school which is rising up, and carrying chemistry into the domains of medicine, are the pioneers of the revolution which is soon to follow. If we look back to what the exact sciences of to-day were in former times, we shall find they were much less perfect then, than medicine is now. Astronomy and chemistry were but astrology and alchemy. If, then, we draw a picture of the future from the progress of the past, we need have no hesitation in saying that chemistry rightly applied, and physiology justly interpreted will, ere many generations pass away, reveal the deepest secrets of diseased action, and although unable to banish death, will



yet enable the practitioner to follow with unerring certainty the various morbid changes occurring in the frame.

77, HARLEY STREET, CAVENDISH SQUARE,  
*March, 1863.*

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## DESCRIPTION OF PLATES AND WOODCUTS.

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### PLATE I.

REPRESENTS the condition of the parts in a fatal case of permanent jaundice, in which both the bile, and pancreatic ducts were completely occluded.

- (a) Atrophied liver.
- (b) Transverse section of the left lobe, showing the mouths of the enormously distended gall-ducts.
- (c) Enlarged gall-bladder.
- (d) Dilated cystic duct.
- (e) Distended hepatic, and common duct.
- (f) Ulceration in duodenum, in the situation of the opening of the gall-duct into the intestines.
- (g) Pancreas with enlarged head (*h*), and enormously distended duct.

### PLATE II.

External surface of the left kidney, denuded of its capsule, in a case of permanent jaundice.

- (a) Small specks of bile pigment deposited in the renal tissue, and blocking up the urine tubes.
- (b) Small abscesses scattered throughout the tissue of the kidney.



## WOODCUTS.

- Fig. 1. Crystals of glycocholate of soda, mag. 90 diam.—Page 8.
- „ 2. Taurocholate of soda, as found in the form of globules of various sizes.—Page 9.
- „ 3. Crystals of cholesterine.—Page 9.
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- „ 6. Globules of leucine.—Page 66.
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- „ 8. (a) Crystals of cystine.  
(b) Hepatic cells, showing entire absence of fat globules.  
(c) Caudate or spindle-shaped cells, from epithelial lining of hepatic ducts —Page 86.

# JAUNDICE:

ITS

## PATHOLOGY AND TREATMENT.

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### INTRODUCTION.

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HAVING entitled this monograph "Jaundice, its Pathology and Treatment," it may, perhaps, be necessary for me to state at the beginning that by so doing it is not to be supposed that I regard jaundice as a disease *per se*. On the contrary, I look upon it in the same light as I do albuminuria, which is not of itself a disease, but only the most prominent symptom of several widely-differing pathological conditions. So also the peculiar state of body characterised by yellow skin, saffron-coloured urine, and pipe-clay stools, is itself but a symptom of morbid action. It may be asked, "Then why do you treat of jaundice as if it were a disease?" To this I reply, "Because, although



the condition called jaundice be merely a manifestation of morbid action, and one, too, requiring neither skill nor experience to detect, the proper comprehension of its true mechanism is of much practical importance to the physician, for without this knowledge it is impossible for him to treat it with any chance of success. Nay, even the remedies for jaundice become dangerous weapons, if unskilfully applied. In fact, it is almost unnecessary to apologise for treating of jaundice as a disease *per se*; for, notwithstanding all that has been written upon the subject, it is universally admitted that the simplicity of its diagnosis is only equalled by the obscurity of its pathology, and the uncertainty of its treatment; and no one at all conversant with the literature of jaundice can be in the least degree surprised at this statement. On the contrary, on glancing at the immense variety of morbid states, and known pathological conditions with which it is associated, he cannot fail to admit its truth.

Some of the pathological conditions are closely allied; others are widely separated—so widely, indeed, that at first sight it is impossible to discover from whence emanates the common symptom. We find jaundice connected with diseases of the liver, of the neighbouring organs, and of the general system. In some diseased conditions,



jaundice presents itself when least expected. At other times it is absent when, apparently, it ought to be present. On the other hand, again, there are cases in which jaundice is evidently merely a symptom, and others in which it seems to be in itself the disease. We have temporary jaundice from transient derangements, and we have permanent jaundice from stationary causes. There are cases in which the cause of jaundice is visible after death to the naked eye. There are others where the minutest research is baffled in ascertaining the cause. That this is no exaggerated view of the case the following table will show :—

JAUNDICE IS MET WITH,

Firstly, IN DISEASES AFFECTING THE LIVER—

- (a) Cancer.
- (b) Tubercle.
- (c) Cirrhosis.
- (d) Inflammation.
- (e) Atrophy.
- (f) Amyloid, and
- (g) Fatty degeneration.

Secondly, IN DISEASES OF THE BILE DUCTS—

- (a) Congenital deficiency.
- (b) Accidental obstruction. The latter arising from gall-stones, hydatids, foreign bodies



(such as cherry-stones and entozoa) entering from the intestines.

- (c) Ulcer of the duodenum.
- (d) Tumours of the pancreas.

Thirdly, IN AFFECTIONS OF OTHER ORGANS OF THE BODY EXERTING AN INFLUENCE ON THE BILIARY SECRETION—

- (a) Diseases of the nervous system.
- (b) Diseases of the lungs.
- (c) Diseases of the heart.
- (d) Imperfect establishment of the extra-uterine circulation (infantile jaundice).
- (e) Dyspepsia.
- (f) Torpidity of the bowels, and consequent accumulation of fæces in transverse colon.
- (g) Pregnancy.

Fourthly, IN A VARIETY OF ZYMOTIC DISEASES—

- (a) Typhus.
- (b) Yellow fever.
- (c) Ague.
- (d) Pyæmia.
- (e) Epidemic jaundice.

Fifthly, AS A RESULT OF THE INJURIOUS EFFECTS OF CERTAIN POISONS—

- (a) Snake bites.

(b) Alcohol.

(c) Chloroform, etc.

Can it be wondered, then, that a state so easily diagnosed is nevertheless so difficult to comprehend?

Notwithstanding the apparent incongruity of the diseases with which the one common symptom of jaundice is associated, I trust to be able to reconcile these discrepancies, and prove that the seeming discord is but "harmony not understood."

All physicians, I think, admit that the peculiar state of the system to which the name of jaundice has been applied, is essentially due to some derangement of the biliary function, the exact nature of the derangement being alone the point of contention. I need not, therefore, waste the time of my readers, either by giving an account of the literature or a detail of the symptoms of jaundice. Even in discussing its pathology, I shall strictly limit myself to the consideration of the opinions at present held by the more advanced of our pathologists; the object of this monograph being, not to pourtray the views of others, but to give a brief *exposé* of my own, and to point out how modern physiology, and chemistry have not only thrown a new light on its pathology, but have also given us a clue to its successful treatment.



Frerichs, the most recent writer on this subject, in his elaborate treatise on diseases of the liver, says that jaundice may result from one of the three following conditions:—

Firstly,—Obstruction to the escape of bile.

Secondly,—Diminished circulation of blood in the liver, and consequent abnormal diffusion; both of these conditions giving rise to an increased imbibition of bile into the blood, and in both cases the liver being more or less directly implicated.

Thirdly,—Obstructed metamorphosis, or a diminished consumption of bile in the blood.\*

From this it is seen, that the pathology of jaundice, according to Frerichs, is very different from what we were formerly taught. For while he has entirely laid aside the theory of jaundice as a result of suppressed secretion, he has introduced two perfectly new elements—namely, abnormal diffusion, and diminished consumption. The latter theory, being, of course, founded on the supposition that bile, after playing its part in the digestive process, is re-absorbed into the circulation, again to perform another function in the animal economy, before its final excretion from the organism as effete matter. The theory of jaundice, hitherto most favoured in England, and which found

\* Frerichs' "Clinical Treatises on Diseases of the Liver." New Sydenham Society's Translation, vol. i. p. 93.



such an able exponent in Dr. Budd, is, that the disease may arise in two ways—firstly, by a mechanical obstruction to the passage of bile into the intestines, and the consequent re-absorption of the detained fluid into the blood; and secondly, by a suppression of the biliary secretion arising from some morbid condition of the liver itself, whereby the biliary ingredients accumulate in the circulation. Now, although I am not prepared to admit the justice of the views held regarding the origin and function of bile, on which these opinions are based, I nevertheless believe that in the following pages I shall be able, by the aid of modern medical science, to prove the correctness of the conclusions themselves. In order to do this, however, it will be necessary for me to begin by making a few remarks on the nature of bile, and the physiology of its secretion.

## ON THE NATURE OF BILE.

IN a few words, bile may be said to be composed of the following substances:—

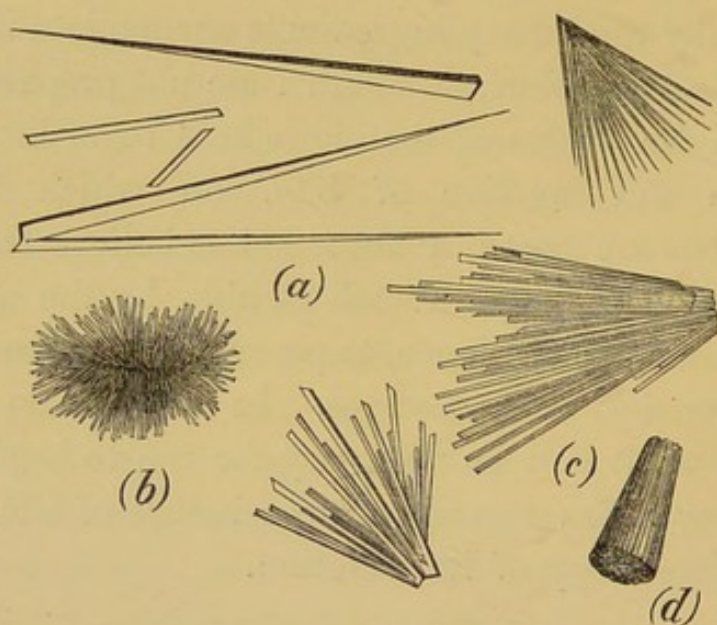
Firstly,—Biliverdine, a green nitrogenized, non-crystallizable colouring matter, analogous to the green colouring matter of plants, and like it, leaving on incineration a distinctly ferruginous ash. This colouring matter appears, like urohæm-



atine, and all other animal pigments, to be a direct derivative of the colouring matter of the blood.\*

Secondly,—Two peculiar substances, named respectively, glycocholic, and taurocholic acid—the former yielding, when in combination with soda, a crystallizable, the latter a non-crystallizable salt.

FIG. 1.



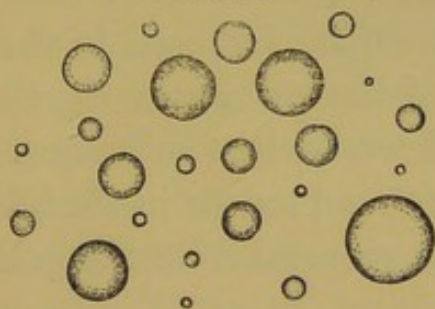
Crystals of Glycocholate of soda, a beautiful polariscopic object. (a) Fine needle-shaped crystals, separated from a rosette-shaped group. (b) Small rosette of crystals. (c) Fan-shaped groups of crystals, which are merely portions of large rosettes that have become broken up. (d) A fragment of a bundle of needle-shaped crystals. Mag. 90 diam.

Taurocholic differs still further from glycocholic acid, in containing a large percentage of sulphur,

\* *Vide* papers by the author on the colouring matter of the urine, Pharm. Journ., November, 1852. "Urohæmatine, and its combination with animal resin." Verh. d. Phys.-Med. Gesellschaft zu Wurzburg, Bd. V. 1854.

and being, under the influence of hydrochloric acid, convertible into taurine, a beautiful white crystalline substance.

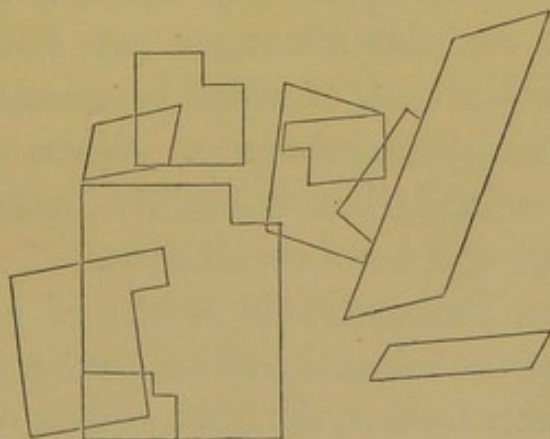
FIG. 2.



Taurocholate of soda is found in the form of fatty-looking globules of various sizes. They differ from fat and oil globules, however, in being soluble in water, and insoluble in alcohol and ether.

Thirdly, — Cholesterine, a crystalline, fatty matter, not, however, peculiar to bile, but found in various tissues, and secretions of the body.

FIG. 3.



Cholesterine crystals appear in the form of fine transparent four-sided plates of various sizes and shapes. The crystals are freely soluble in hot alcohol, from which they are re-deposited on cooling.



Fourthly,—A brown resinous substance resembling, in appearance and consistence, shoemaker's wax.

Fifthly,—Among the constituents of the bile, I may mention sugar, for both in the normal bile of man, and of the lower animals, the ox, and the dog, I have detected that substance. On one occasion, I even found *torulæ* in the bile twenty-four hours after its removal from the gall-bladder of a healthy dog.

Sixthly, and lastly,—a quantity of inorganic matter, consisting chiefly of soda, potash, and iron.

The specific gravity of bile fluctuates, of course, with the percentage of solid matter it contains. From my own observations, I consider that healthy human bile has an average specific gravity of 1020, and contains about six per cent. of solid matter, five per cent. of which is organic, and one per cent. inorganic substance. When fresh, bile is almost neutral; but it rapidly undergoes decomposition, and becomes alkaline.

In colour, human bile is usually of a brownish yellow hue; the colour, however, varies with its degree of concentration, the kind of food taken, and the state of the system. As regards the effect of food, if we may be allowed to form an opinion from experiments on dogs, it may be said that, as a



rule, animal food tends to give bile a yellow, vegetable food a green, tint.

Next, as regards the manner in which bile is secreted. For a long time it was thought, and, indeed, some people still think, that bile exists pre-formed in the blood, and that the liver only excretes it, as the kidneys excrete the urinary ingredients. Another class, running to the opposite extreme, believe that the liver is not merely the excretive, but also the formative organ of the bile. It appears to me, however, that neither of these extreme views is correct, and that the truth lies between the two.

It is, in fact, not at all difficult to prove that the liver manufactures certain biliary constituents, while it merely excretes others. Thus, for example, the two substances glycocholic and taurocholic acids are never to be found either in the blood, tissues, or fluids of the healthy organism, with the single exception of those of the liver and gall-bladder; and after extirpation of the liver neither acid is to be found in the body at all. On the other hand, such substances as cholesterine and biliverdine, are not peculiar to the liver or its secretion, but are the products of several organs, and are always to be detected in the blood, independently of the presence or absence of the liver. These facts, therefore, clearly show that the liver



is both a formative and excretive organ to some, and an excretive only to others, of the biliary constituents.

Lastly, the general opinion is that the secretion intermits, and, like the gastric, and pancreatic juices, bile is only formed during digestion. Were it so, however, where would be the necessity for a gall-bladder? Is it not to store up the secretion formed in the intervals of digestion, and to retain it until it is required? No doubt there are several animals, such as the horse, and the deer, that possess no gall-bladders; but there is undoubtedly in them some special arrangement of the digestive apparatus, rendering the presence of a gall-bladder unnecessary. In fact, it is easily shown that the biliary secretion in ordinary cases is continuous; for if in an animal possessing a gall-bladder a biliary fistula be established, and the secretion of bile carefully watched, it will be found that at no period of the day does it entirely intermit, although it is more active at one time than at another, the minimum of its activity being during sleep—the maximum during active digestion. The absolute quantity of bile secreted in the twenty-four hours is tolerably uniform, although the daily amount is slightly influenced by the kind of food.\*

\* Arnold found that dogs secreted more bile on a bread, than on an animal diet. "Zur Physiologie der Galle," Mannheim, 1854.



## IS BILE ESSENTIAL TO LIFE?

Several physiologists have given it as their opinion that bile is not essential to life, for animals have lived for many months after the artificial establishment of a biliary fistula, through which the bile was allowed to flow away, and be lost to the animal. Now, although this is perfectly true, yet it is at the same time evident that the uses of the bile cannot altogether be dispensed with, for all the animals with a biliary fistula lose flesh, become emaciated, and weak; the hair has a tendency to fall off, the bowels to become irregular; and a great and an almost constant discharge of foul-smelling gases takes place from the intestinal canal. At length, after a shorter or longer period, the animal sinks, and dies. The fatal termination can, however, be retarded by allowing him an additional quantity of nourishing food, for death from want of bile, as is too often seen in the human subject, is nothing else than death from slow starvation. The fact just related regarding the beneficial effects of an additional quantity of food in prolonging life, should never be lost sight of in the treatment of cases of obstruction of the gall-ducts, for, by attending to this circumstance, it is often in the power of the medical man to keep his patient alive for a considerable length of time.



It may perhaps not be out of place if I here briefly enumerate the chief uses of bile in the animal economy. In order to live, not only must the individual particles of our frames die, but they must be continually replaced by new materials of a similar kind ; and for the accomplishment of this important end, nature has endowed animals with a digestive apparatus in which their food undergoes the various physical, and chemical changes necessary to its absorption, and assimilation. In the animal laboratory or digestive apparatus there are five important agents constantly at work—saliva, gastric juice, bile, pancreatic fluid, and intestinal secretion, and each of these agents has a special and definite office to perform in the elaboration of the food.\* At present, however, I must limit myself entirely to the consideration of bile.

Bile is the first digestive agent with which the food comes in contact on leaving the stomach and entering the intestines, and immediately on the acid chyme mixing with the alkaline bile, a white flocculent emulsion is formed, which emulsion has been described by many writers as a precipitation of the albuminose (digested albumen). Later

\* For an explanation of these offices, see the author's article on "The Chemistry of Digestion," in the "British and Foreign Quarterly Review," January, 1860.



researches by myself and others have, however, shown that it is not the bile which precipitates the albuminose, but the acid of the chyme, which in reality sets free certain ingredients of the alkaline bile. In the majority of cases there is not even a true precipitation, for on throwing the milky-looking mixture upon a filter, I found that almost nothing remained behind, and the filtrate was nearly as white as the original liquid. Further, if the albuminose be separated from the chyme, and the chyme then brought into contact with the bile, the same flocculent-looking milkiness still appears. Nay, more, on adding equal parts of sheep's bile (fresh) to gastric juice drawn from a dog's stomach in full digestion, the apparent flocculent precipitate still appeared, although the acidity of the gastric juice remained unneutralized; and on throwing the whole into a filter, I found that the liquid that drained through was as milky and flocculent-looking as the original. The office of bile in the digestive process is neither to act on the albuminous\* nor amylaceous portions

\* In speaking of the properties of the bile, I may mention that, although bile has no digestive power (properly speaking) over albuminous substances, yet, when injected into the subcutaneous cellular tissue of a healthy animal, it eats its way out through the skin, just as gastric juice or lactic acid does under similar circumstances. Even the muscles with which it comes in contact appear to be eaten away.



of our food; its chief action being to assist in the absorption of fats. When bile is mixed with neutral fat, little change is observed, but when brought in contact with the fatty acids, an immediate emulsion takes place. Lenz and Marcet\* pointed out how the neutral fats of our food are transformed into fatty acids during their sojourn in the stomach; and Bidder and Schmidt† illustrated by experiments on dogs the important part played by the bile in their absorption. A dog, which in its normal condition absorbed on an average 7 grains of fat for every 2 pounds of its weight, absorbed only 3, or even as little as 1 grain, after the bile was prevented entering the intestines, in consequence of a ligature being applied to the gall-duct.

Further, these last-named observers found that, while the chyle in the thoracic duct of a healthy dog contains 32 parts of fat per thousand, that in the thoracic duct of a dog with a ligatured gall-duct, contains only 2 parts per thousand. These facts clearly prove that bile plays an important part in the absorption of the fatty portion of our food. Next comes the question, "In what manner does bile aid in the absorption of fatty matter?"

\* *Vide* a Discourse on the Chemistry of Digestion, by Dr. Marcet. Journ. of the Chem. Soc., Oct. 1862.

† "Die Verdauungssäfte und der Stoffwechsel." Leipzig, 1852.



As is well known, fats or oils have no tendency to mix with water, and hence diosmose between an aqueous and an oily fluid is next to impossible. Matteucci has, however, shown that if an animal membrane be moistened on both sides with a weak solution of potash, it allows oil to pass through it. It has also been observed, that when the intestine is moistened with bile, it allows oil to pass through, which would not otherwise be the case. To illustrate this property of bile, I performed the following experiments:—

Firstly,—A clean piece of duodenum was filled with oil, ligatured at both ends, and suspended in water, holding in solution a small quantity of albumen. (The albumen was added to the water merely to imitate slightly the albuminous blood.) On examination, twenty-four hours later, no oil was found to have escaped through the intestinal walls.

Secondly,—A second portion of intestine had its internal surface moistened with sheep's bile before the introduction of the oil. It was then treated in the same manner as the preceding, and on being examined after the lapse of twenty-four hours, a small quantity of the oil was found to have penetrated through the intestine.

Thirdly,—Into a third portion of intestine was poured equal parts of sheep's bile, and chyme obtained from a dog in full digestion, through a



fistulous opening into its stomach. After being treated for the same length of time, and in precisely the same manner as the others, evident signs of the oily matters of the chyme having passed through the walls of the intestine were obtained, for they were seen as a scum floating on the surface of the albuminous water. Moreover, the fatty matters were not in the form of pure oil, but of a soapy substance.

The bile is thus seen to possess one of the more remarkable properties of the pancreatic juice. There is this important difference between the action of these two secretions on fats, however, that while bile merely emulsions and saponifies that portion of our food which enters the duodenum in the form of fatty acids, pancreatic juice, on the other hand, possesses the power, not only of emulsifying and saponifying the fatty acids, but also the neutral fats; indeed, its power seems chiefly to be exerted upon the latter. Hence it appears that both secretions are in a measure necessary to the complete digestion and absorption of the oleaginous constituents of our food.

On one occasion, while experimenting with bile at University College, I was surprised to hear Minton, the servant who was assisting me, say, that while he was travelling with Sir Andrew Smith in South Africa, he had oftentimes seen the



Caffres drink bile direct from the gall-bladders of the animals killed by the European party, and that, while passing the gall-bladder round to each other, they would rub their stomachs and say,—“Mooé-ka-kolla,” signifying thereby, that it was very good. It certainly seems very extraordinary that any human being should not only drink, but drink with pleasure, a liquid so bitter and nauseating as bile. Perhaps the poor Caffres, however, drank the sickening tasted bile for the same reasons as the cattle in Caffreland, at certain periods of the year, go thousands of miles to drink at the salt-springs. There being scarcely any chloride of sodium in the earth, there is insufficient for the animal requirements in the herbage on which they feed, and they are forced to supply the deficiency by artificial means. Bile contains a large percentage of soda, and perhaps the Caffres drink it in order to obtain that substance, just as the animals drink the brackish water of the salt licks, feeling that it agrees with them, without knowing why.

## THE MECHANISM OF JAUNDICE.

As said in the beginning of this paper, I believe, the pathology of jaundice may be embodied under the two heads, jaundice from suppression



of the biliary functions, and jaundice from re-absorption of the secreted but retained bile. These are at best, however, but vague terms, and in order to make the pathology of jaundice somewhat more definite it will be necessary for me to subdivide these two great classes in the following manner:—

(CLASS A.)—JAUNDICE FROM SUPPRESSION.

Arising from:—

- (1) Enervation.
- (2) Disordered hepatic circulation.
- (3) Absence of secreting substance.

(CLASS B.)—JAUNDICE FROM RE-ABSORPTION.

Arising from:—

- (1) Congenital deficiency of bile-ducts.
- (2) Accidental obstruction of bile-ducts.

I shall now try to point out the pathology of these different states, and see how far they are able to explain the occurrence of jaundice under the various conditions already alluded to.

JAUNDICE FROM SUPPRESSION.

Although there can be no misunderstanding the meaning of the term “jaundice from suppression,” there may, nevertheless, be some difficulty in comprehending how the skin becomes yellow, and the urine high coloured, when the secretion



of bile is arrested. In order to explain how this occurs, it will be necessary to recall to mind what was said regarding the nature of the biliary secretion. It will be remembered that I began by saying, that while some of the constituents of the bile are generated in the liver itself, there are others that exist, pre-formed in the blood.

If this view of the physiology of the biliary secretion be correct, it is perfectly evident that when the secretion of bile is arrested, those substances which the liver generates will be entirely wanting, while those which it merely excretes from the blood will accumulate there as soon as their excretion is prevented; just as urea accumulates in the circulation when its elimination by the kidneys is stopped. Hence it is that, as soon as the biliary secretion is in abeyance, biliverdine accumulates in the blood (until the serum is as it were completely saturated with the pigment), from which it exudes and stains the tissues, and produces the colour we term jaundice. At the same time, or even before the skin becomes yellow, the urine assumes a saffron tint in consequence of the elimination of the colouring matter by the kidneys.\* From this it will be seen that I regard

\* The true order of the occurrence of these changes is:—On the second day the urine becomes high-coloured; in a day or two later the skin assumes a yellow tint; and, in very severe cases,



the yellow skin and high-coloured urine of jaundice as simply due to the deranged secretion of biliverdine, quite independent of the presence or absence of the other constituents of the bile, the effects produced by which will be referred to elsewhere. Meanwhile we shall separately consider the further pathology of the three subdivisions of jaundice arising from suppression.

#### JAUNDICE AS A RESULT OF ENERVATION.

It is now a well-established fact that all secretions are under the direct influence of the nervous system. Stimulate a nerve supplying a gland, and secretion is accelerated; stop the nervous action, and secretion is as instantaneously arrested. Again, just in the same way as volition can produce or suspend muscular movement, mental influence can hasten or retard glandular secretion. As an illustration of this fact, I need only call to mind the influence the mere sight of food has in exciting the salivary secretion, and the effect of bad news in arresting it. Exactly the same influence as is here alluded to, is exerted by the mind over the biliary function. If, for example,

within the first week or two, the sweat, the milk, the tears, the sputa, and the serum in the thoracic and abdominal cavities, become of a more or less decided yellow hue.



as Bernard first observed, a dog with a biliary fistula be caressed, the secretion of bile is actively continued; if, on the other hand, the animal be suddenly ill-used, the secretion of bile is instantly arrested. If he be again caressed, the secretion is re-established, and the bile flows drop by drop from the end of the cannula. Here the influence is entirely produced through the intervention of the nervous system; and if such effects as are above described occur in the dog, we can surely have little difficulty in understanding how the biliary secretion can be influenced in the highly-developed organization of the human being. Indeed, every one must have felt how quickly sad tidings received during a meal not only destroy the appetite and retard digestion, but occasionally alter the complexion. This effect, that all of us must have experienced in a slight degree in our own persons, several may have observed to a greater extent in the persons of others, even to the production of well-marked jaundice. At this very time I have under my care a young married lady, who during the last two years has twice suffered from an attack of jaundice induced by witnessing her child in convulsions, and this I regard as an example of jaundice from enervation.

One of the reasons, no doubt, why jaundice does not more frequently follow upon mental emotion is



simply on account of a certain amount of pigment being required in order to produce a visible tinging of the body, and it seldom happens that the emotional effect on the biliary secretion is sufficiently permanent to permit of the requisite amount of pigment accumulating in the blood. The reason, too, why mental emotion is more apt to cause jaundice immediately after a meal is, as will afterwards be better understood, on account of the congested state of the liver at that time favouring the stoppage of the secretion. A blow on the head, which is now and then observed to be suddenly followed by jaundice, acts, I believe, in the same way as fright, namely, by paralyzing the nerve force required for the continuance of the biliary secretion.

I now pass on to the consideration of the pathology of the second kind of jaundice from suppression, namely, jaundice resulting from hepatic congestion.

#### JAUNDICE ARISING FROM HEPATIC CONGESTION.

This is one of the most common causes of the disease; but as there are two kinds of hepatic congestion—active and passive—it will be necessary for me to make a further subdivision, and consider each of these separately.



*Jaundice the Result of Active Congestion.*

The mechanism of jaundice resulting from active congestion of the liver is readily explained on physiological grounds.

The congested condition of any gland is unfavourable to secretion. We all know, for example, that congestion of the kidney is accompanied by a suppression of the urinary secretion, and that the secretion is re-established as the congested condition of the organ diminishes. The suppression of the renal secretion is no doubt due to the engorged capillaries pressing upon the secreting structure, and ultimate ramifications of the urine tubes, and thereby annulling their functions. A similar explanation is equally applicable to the biliary secretion; and just as it happens in the case of the kidney, that it is exceedingly rare for a total suppression of its functions to take place, so with the liver it seldom happens that the congestion is sufficiently severe to induce complete arrest of the biliary secretion. We find, therefore, that although there may be yellowness of the skin and high-coloured urine in such cases, pipe-clay stools are frequently absent, sufficient bile to tinge the fæces still finding its way into the intestines.

Undoubtedly it must have occurred to many of my readers, that jaundice is frequently absent in



cases of acute inflammation of the liver, even running on to suppuration, and that the foregoing theory of the pathology of such cases is therefore insufficient. At one time I was puzzled to explain this apparent anomaly, but on subsequent investigation the true cause became apparent, and instead of the above fact detracting from, it tended rather to strengthen the theory. If, for example, we closely examine cases of acute hepatitis without jaundice, we find they are those in which only a portion of the liver is affected. It matters not whether it be one lobe or two, the surface or the centre of the organ, the disease is invariably circumscribed; and there is enough hepatic tissue left in a sufficiently normal condition to prevent the constituents of the bile accumulating in the blood, and producing jaundice. This may even occur, as I have myself observed, when the disease has run on to suppuration.

The most typical example of jaundice as the result of active congestion, is to be found in those cases where it supervenes on an attack of hepatitis, such as is met with in hot climates, where indolent habits and high living favour portal congestion. It is occasionally met with in England, however, and is frequently associated with gastric derangement.

I had occasion to witness a good example of



this form of disease in the person of a French gentleman, who was brought to me seven days after his arrival in England, on account of his skin having assumed a most intense yellow hue. It appeared that he had come to England on a visit to some of his friends, and rather enjoying the novelty of an English table, indulged too freely in a quantity and quality of food to which he had hitherto been a stranger. The consequence was, that within three days after his arrival he began to suffer from hepatic tenderness, and dyspeptic symptoms; the skin at the same time assumed a dusky hue, which soon merged into a decided yellowness. These symptoms were accompanied by pipe-clay stools and saffron-coloured urine; on the latter being tested it gave a distinct bile pigment, but no bile acid reaction—a point which I shall afterwards have occasion to show, is of a certain diagnostic value in obscure cases of jaundice. This gentleman, under the influence of benzoic acid, perfectly recovered his normal complexion in the short space of a week.

There is another form of jaundice from active congestion, viz., that due to the presence of zymotic disease, such as ague, typhus, and other fevers. As an illustration of this kind of affection, I shall cite one arising from the first of these causes, namely, ague. And the best example I



can give is one that has recently fallen under my notice, and which occurred in the person of a member of our own profession. The gentleman was for several years surgeon to one of our large colonial hospitals, but in consequence of repeated attacks of intermittent fever, was forced to resign the appointment, as well as a lucrative practice, and return to England. He has now been at home for two years, and although his general health has much improved, still suffers from occasional attacks of his old enemy. On consulting me regarding his case several months ago, he mentioned, that while suffering from the above-named attacks, he occasionally suddenly passed five or six ounces of urine as dark as chocolate, and this would recur perhaps once in twenty-four hours, during two or three days, and then as suddenly disappear. This urinary symptom being an unusual one, I requested him to send me on the next occasion a specimen of the fluid. In the beginning of last November\* I received three samples of urine, one passed at eight A.M., which was clear, pale, of a specific gravity of 1025, of an acid reaction, deposited no lithates, and contained no albumen, being in fact normal in every respect; another quantity passed at two P.M., of

\* This was written last year, and therefore refers to November, 1861.



a chocolate brown colour, opaque, turbid, having a specific gravity of 1032, of an acid reaction, depositing lithates, containing albumen,\* some sugar, and a large excess of urea (3·6 per cent.) and urohæmatine; a third sample passed at night, of a specific gravity of 1021, also with an acid reaction, depositing lithates in small quantity, but containing no albumen. The percentage of urea in this urine was exactly one-half (namely, 1·8) of what it was in the preceding specimen passed at two P.M.

The varying conditions of these three urines clearly pointed to intense congestion of the chylopoietic viscera, of a transient and periodic character. Suiting the practice to the theory, mercurials were taken by this gentleman in order to remove the congestion of the chylopoietic viscera, and with the most favourable results, for, as I afterwards learned, the jaundice and other disagreeable symptoms soon disappeared.

*Jaundice the Result of Passive Congestion of the Liver.*

In this case the congestion, instead of arising from an increased flow of blood to the liver, as

\* When examined with the microscope, this specimen of urine was found to contain a large quantity of nucleated epithelium, and granular cells; free granules of a hæmatine colour, granular tube-casts, and a quantity of mucus; while the morning and evening urines were perfectly free of any such substances.



in the preceding, is the result of some cause impeding the outward flow of blood from the liver. Thus for example, passive hepatic congestion may arise from valvular disease of the heart, or from any pulmonary affection obstructing the circulation of blood through the lungs (pneumonia, &c.). Jaundice from the passive form of hepatic congestion, is not so common as jaundice from the active form, in consequence of the former being, as a rule, much slighter than the latter. Its pathology is, however, I believe, exactly the same, viz. the result of the engorged hepatic capillaries compressing the secreting cells and tubes, and thereby annulling their functions. Such being the case, it is unnecessary for me to do more than merely allude to this cause of jaundice.

It may, perhaps, be asked—"If the foregoing statements regarding the pathology of jaundice from congestion be correct, how does it happen that it is not present in every severe case of gastric derangement, fever, heart-disease, &c.?" This question is easily answered, for as Dr. Budd has clearly put it, while speaking of the action of medicines upon the liver—"In most persons, perhaps, a portion of the liver may waste or become less active without sensible derangement of health, they have more liver, as they have more lung, than is absolutely necessary. In others, on the



contrary, the liver, from natural conformation, seems just capable of effecting its purpose under favourable circumstances." Persons inheriting this feebleness of liver, "or in whom, in consequence of disease, a portion of the liver has atrophied, or the secreting element of the liver has been damaged, may suffer little inconvenience as long as they are placed in favourable circumstances, and observe those rules which such a condition requires;" but as soon as the balance of their hepatic circulation is disturbed by causes like those above mentioned, jaundice makes its appearance; such patients being, as Dr. Budd says, "born with a tendency to bilious derangements."\*

JAUNDICE AS A RESULT OF SUPPRESSION CONSEQUENT UPON ABSENCE OF THE SECRETING SUBSTANCE.

The pathology of this state is self-evident, for wherever secreting substance is wanting, secretion cannot take place. If then, the tissue which secretes bile be destroyed or transformed by disease, the biliary function must be suspended, and the ingredients which it is the office of such structure to separate from the blood, will accumulate in the circulation, and give rise to the

\* Diseases of the Liver, p. 55.



usual chain of results following suppression of the biliary secretion.

In cancer, tubercle, fatty and amyloid degeneration of the liver, jaundice arises from the above-named cause. In these diseases it is not, however, a constant symptom, and this is simply on account of there being usually sufficient healthy tissue left to enable the biliary secretion to be carried on. If the cancer, or other morbid product, occupied the whole place of the secreting tissue, the biliary function could no more be carried on by such product, than by the same product occupying another organ of the body. In cases of jaundice arising from absence of the secreting substance, the amount of the jaundice depends on another cause besides the mere extent of the morbid deposit. This is its situation. A large amount of diseased tissue may exist in certain portions of the liver, and yet fail to produce jaundice, while a much smaller amount of the same diseased tissue, placed in another situation, may induce it. Should the morbid deposit, for example, be so placed as readily to interrupt the flow of the secreted bile, jaundice may rapidly occur, and be due as much to the re-absorption of the secreted bile, as to the suppression of the biliary secretion. This is, indeed, the true explanation of the fact, that diseases affecting the



concave, are much more frequently accompanied with jaundice, than those attacking the convex surface of the liver. I might have chosen what at first sight appears a more typical example of absence of secreting structure, namely, a case of acute atrophy of the liver; for in such cases the hepatic tissues sometimes dwindle down in the course of a few days to less than a quarter of their original bulk, and give rise to intense jaundice. But in such cases there does not appear to be a total arrest of the secretion, until the very last stage of the disease, if it even occurs then; and besides, if I dare form an opinion from one case, I should say that, in consequence of the rapid disorganization of the parenchyma of the liver, the circulation in the organ becomes much disturbed, and gives rise to what Frerichs terms disordered diffusion. So that in cases of acute atrophy of the liver, the jaundice, although chiefly due to suppression, is complicated with re-absorption of the bile, as was proved in a case I examined, by finding in the urine, not only those products which are merely excreted from the blood, but also some of those which are generated in the liver itself. It will be necessary for me, therefore, to go more fully into this form of jaundice than I have done in any of the preceding forms of the disease.



## JAUNDICE ARISING FROM ACUTE ATROPHY OF THE LIVER.

Acute, or yellow atrophy of the liver, is one of the most formidable of human diseases. It is sudden in its onset, rapid in its course, fatal in its termination. It is more common in women than in men; seldom attacks those above thirty years of age, and occurs most frequently in the earlier months of pregnancy. The immediate exciting cause of this strange disease appears to be, in the majority of cases, mental depression. The symptoms usually observed are jaundice, rapidly followed by sickness, and vomiting; by febrile excitement, and cerebral disturbance.

As the disease advances, the hepatic dulness diminishes; the urine becomes scanty, and high-coloured; the bowels confined. Extravasations of blood take place under the skin; and hæmorrhages from the nose, vagina, or bowels are frequently observed. Lastly, delirium, or coma, generally closes the scene, within a week after the commencement of the violent symptoms, and within a month after the appearance of simple jaundice. Frerichs, who has so well described these cases, even says, "that in the severest forms, the disease may run its course, and end fatally within twenty-four hours."\*

\* "Clinical Treatises on Diseases of the Liver," vol. i. p. 197.



All cases of acute atrophy of the liver are, fortunately, not necessarily fatal. In some the violent symptoms gradually disappear, and recovery takes place after free evacuation of the bowels.

In every case of suspected acute atrophy of the liver, the urine ought to be carefully examined for tyrosine, and leucine, two abnormal products, which, according to Frerichs, are never absent. Some remarks on the diagnostic value of these substances will be found at page 62.

Through the kindness of Dr. Wilks, I had the opportunity of examining the liver, and analysing the urine, in a typical case of acute atrophy, which he reported in the Pathological Society's "Transactions," vol. xiii. p. 107. The brief history of the case is as follows:—E. K., aged seventeen, a married woman, in the third month of pregnancy, was seized with a bilious attack, and jaundice, after having a violent quarrel with her husband, who accused her with infidelity. The patient was first under the care of Mr. Bisshopp, of South Lambeth, who found her suffering from jaundice, accompanied by some febrile symptoms, and vomiting. In two days she became delirious, had violent screaming, and convulsive fits, which were rapidly followed by unconsciousness. Next day the patient was seen by Dr. Wilks; she was then quite insensible, with slight stertorous breathing,



and foam on the lips. The pupils were moderately dilated, and sensible to light. The pulse 120. The hepatic dulness reduced to a narrow band over the lower ribs. No urine had passed for twenty-four hours; a catheter was therefore introduced, and twelve ounces of clear bilious-looking fluid were drawn off. This urine I had the opportunity of analysing a few days afterwards. It was then of a yellow-ochre colour, and contained a considerable deposit.

The analysis gave:

Specific gravity	. . . . .	1028
Reaction	. . . . .	acid (?)

IN 1000 PARTS.

Water	. . . . .	948.860
Solids	{ organic inorganic }	51.138
Urea	. . . . .	30.000
Uric acid	. . . . .	0.375
Resin and mucus	. . . . .	
Bile, colouring matter, and acids	}	
Urohæmatine		
Leucine, and tyrosine		14.575
Inorganic salts	. . . . .	6.188

The biliary acids (contrary to what Frerichs found in some of his cases) were present in this urine in fair quantity. With Pettenkofer's test (sulphuric acid and sugar) a decided purple colour was obtained.

When a portion of the urine was concentrated, and allowed to crystallize slowly, beautiful crystals of both tyrosine, and leucine were detected in it by means of the microscope. The purified urine also showed the presence of sugar in small quantity. When the organic solids were burned, they had a strong odour, and gave off a smoky *flame*, thereby showing that the urine contained a considerable quantity of fatty resin.

As calculating the constituents of the urine by *percentage* is a very unsatisfactory method for scientific purposes, it may be useful for me to give the analysis of the same urine as calculated for twenty-four hours, viz., twelve ounces, the amount drawn from the bladder shortly before death. In that case the analysis gives :

24 HOURS' URINE.				
Quantity . . . . .				372.00 c. c.
Specific gravity . . . . .				1028
Reaction . . . . .				acid (?)
Solids (total) . . . . .				19.038 grammes.
Urea . . . . .				11.160 „
Uric acid . . . . .				0.139 „
Resin, and mucus . . . . .	}			
Bile pigment, and acids . . . . .				
Urohæmatine . . . . .			5.441	„
Tyrosine, and leucine . . . . .				
Inorganic salts . . . . .			2.298	„

During the night before her death, the patient



aborted, and lost a considerable quantity of blood by the vagina. The whole duration of the disease was merely six days, and the more urgent symptoms only manifested themselves two days before the fatal termination.

After death the liver was found to be very small in size, not exceeding, as was supposed,  $1\frac{1}{2}$  pound in weight. It was deeply stained yellow, and its cells were found to be small, and broken up; not an entire cell could be detected by either Dr. Wilks or myself—nothing, indeed, but a quantity of *débris* of hepatic tissue, and fat. The gall-bladder was contracted, and contained only a little mucus; the urinary-bladder was empty.

Although jaundice the result of acute atrophy of the liver, might be thought to be a typical example of jaundice arising from a suppression of the biliary function—the diminution in secreting substance naturally inducing a diminution in secreting power—I have, as was before said, been led to view it differently; because, although less bile than usual is secreted, there is nevertheless nothing like an entire suppression of the biliary function, as is proved,—

Firstly,—By the absence of pipe-clay stools.

Secondly,—By the deep staining of the hepatic tissue with bile pigment, just as occurs in jaundice the result of obstruction.



Thirdly,—By the presence of the biliary acids in the urine.

Fourthly,—and lastly, the violent symptoms of bile-poisoning lead to the same conclusion, for it is not bile pigment, but the bile acids, that induce the fatal symptoms of bile-poisoning.\*

### CLASS B.

#### THE MECHANISM OF JAUNDICE ARISING FROM THE RE-ABSORPTION OF THE SECRETED, BUT RETAINED BILE.

In cases of this kind, the obstruction is not usually to be found within the liver itself, but in the ducts after their exit from the hepatic organ. The seat of the obstruction, too, is much more frequently found near to, or at the termination of the common duct, than close to the liver. The obstruction may be of three kinds :—

\* Six grains of pure glycocholate of soda killed a small dog, into whose femoral vein I injected it, in the course of two hours. In experimenting on animals, I have made the curious observation, that although bile has the property of retarding or arresting putrefaction, both in the intestinal canal, and out of the body, yet, when injected into the subcutaneous cellular tissue of a healthy animal, it causes the surrounding tissues to decompose, and become foetid, and an artificial disease is thereby set up, whose most peculiar feature is the engendering of a rapid putrefaction of the body after death.



Firstly,—A congenital deficiency of the bile-ducts.

Secondly,—An accidental obstruction in the course of the ducts, as from gall-stones, hydatids, or the entrance of foreign bodies from the intestines.

Thirdly,—From closure of the outlet of the common duct, as, for example, from the pressure of the pregnant uterus, or distended transverse colon, or from organic disease of the pancreas, or neighbouring organs.

First, as regards cases of jaundice from congenital deficiency of the ducts. Cases of this kind are rare. The best with which I am acquainted is the one that was brought before the Pathological Society last year, by Dr. Wilks. "The child had never passed any meconium, the motions always being of a white colour. When a fortnight old, jaundice came on, and continued until death, at the age of six weeks. After death, the liver was found of a dark green colour, and, apparently, the gall-bladder was absent. On further examination, however, the cellular tissue, which appeared to occupy its place, was found to be occupied by a small canal, just large enough to contain a bristle; to this, however, no outlet could be found, and on endeavouring to discover the hepatic ducts, these, in like manner, could not be made



out. The opening of the common duct in the duodenum was natural, but no hepatic duct could be found joining the pancreatic. It appeared, therefore, as if the larger ducts had become shrunk and obliterated.”\*

Through the kindness of Dr. Wilks, I had the opportunity of making a microscopical examination of the liver. The hepatic cells were very small in size, much broken up; very few possessed nuclei, and all were deeply tinged with brownish yellow colouring matter. Scattered throughout the hepatic tissue, I found numbers of well-formed cholesterine crystals, like those represented in Fig. 3.

I must here mention, that jaundice does not necessarily follow upon absence of the gall-bladder; just as in the horse, the deer, the rat, and other animals that possess no gall-bladders, the biliary function is perfectly well carried on, so it may be in the human subject,\* labouring under a congenital or accidental deficiency of the gall-bladder. In such cases, the hepatic ducts are pervious, and consequently the secreted bile finds no difficulty in reaching the intestines. In the “Edinburgh Medical Journal” (May, 1861, p. 1045,) Dr. Alexander Simpson reports a case of

\* “Medical Times and Gazette,” 29th March, 1862.



this kind occurring in a child, which died when only a few weeks old. There was no trace of the existence of a gall-bladder; but on laying open the duodenum, the orifice of the bile-duct was at once seen in its ordinary situation, and a drop of pale bile was expressed from it. On tracing the duct to the liver, it was found to pass up undivided into the horizontal fissure, where it at once broke up and branched into the hepatic tissue of the right, and left lobes.

I shall delay entering into an explanation of the mechanism of jaundice from obstruction, until I come to the consideration of what may be termed *Permanent Jaundice*, as in that case one explanation will do for all.

#### JAUNDICE AS A RESULT OF THE ACCIDENTAL OBSTRUCTION OF THE BILE-DUCTS.

The second class of cases, namely, those in which the obstruction is in the course of the ducts, are of frequent occurrence, and in them the jaundiced state is usually merely transient, for no sooner has the obstruction been removed, than the jaundice begins to disappear. The most common cases of this kind are those arising from gall-stones. As every one is familiar with their history, I may merely mention, that we may have gall-stones, and even all the most painful



symptoms of gall-stones, without the slightest trace of jaundice. This, I believe, arises in the following manner:—

Firstly,—The majority of gall-stones are formed in the gall-bladder; their formation being due to the accidental deposition of the less soluble parts of the bile, either as a consequence of these ingredients being present in excess, or in consequence of the solvent, whose duty it is to retain them in solution, being in reduced quantity. The deposition or formation of gall-stones follows exactly the same law as the deposition or formation of stone in the bladder.

Secondly,—In some cases the gall-stone, or stones—for there may be many, even hundreds, remain in the gall-bladder during the whole life of the individual, without giving rise to any disagreeable results, either as regards pain, or jaundice. In other cases, the gall-stones—and this usually happens when they are small—get into the cystic duct, and become lodged there; and in such a case, although the patient may suffer intense pain, there is still no jaundice. Moreover, it is not until the stone or stones have passed down into the common bile-duct, that jaundice is at all likely to be induced by them. For while a stone remains in the cystic duct, although it may completely block it up, and effectually prevent the bile either



entering into or escaping from the gall-bladder, yet, as in this situation it cannot offer any obstacle to the direct flow of the biliary secretion from the hepatic tissue into the intestines, there is no retention, and consequent absorption of bile. In fact, the presence of the stone in this position, in as far as the biliary function is concerned, only reduces the patient to the state of a person in whom the gall-bladder is accidentally absent; or to that of a horse, or other animal, in which the absence of the gall-bladder is a normal condition.

Thirdly,—There are yet other ways in which gall-stones may give rise to great discomfort, and even imperil life, without inducing jaundice. For example, a calculus may remain in the gall-bladder until it attains a very large size, and then ulcerate its way into the stomach, intestines,\* peritoneal cavity, or even out of the body through an opening in the abdominal parietes.†

In fact, jaundice only appears as a complication of gall-stones when they chance to block up the common duct, and thereby prevent the bile entering the intestinal canal. Hence, also, the reason

\* *Vide* a case of this kind published by the author in the Pathological Society's "Transactions" for 1857, p. 235.

† *Vide* a case published by Mr. Hinton in the "Brit. Med. Journ." of August 4th, 1860, p. 603, and one by Mr. Sympson in the same Journal of the 7th February, 1863, p. 139.



why jaundice, as a result of gall-stones, is more frequently transient than permanent. If it chances to become permanent, it sooner or later leads to a fatal termination—usually within eighteen months after complete obstruction. Lastly, it may be mentioned that, although gall-stones are liable to form in almost every constitution, yet it is generally considered that they are most frequent in persons of the tubercular, cancerous, and gouty diathesis, either hereditary or acquired.

There are other substances besides gall-stones which, by their accidental presence in the bile-ducts, may give rise to jaundice. Thus, for example, foreign bodies, such as cherry-stones, have found their way from the intestine into the bile-duct, and given rise to jaundice. Intestinal worms have been observed to do the same thing, and recently an interesting case of jaundice, occurring in a girl aged 16, who died after a few weeks' illness, has been reported, which resulted from the presence of hydatids in the ductus hepaticus, and ductus communis choledochus.\* Hydatids of the liver itself seldom give rise to jaundice, their position being usually such as not to interfere with the biliary function.

There are still other cases where we find tran-

\* Dr. Dickinson has reported this case in the Pathological Society's "Transactions," p. 104, vol. xiii. 1862.



sient jaundice arising from accidental obstruction of the bile-ducts; but in them, instead of the closure of the ducts resulting from plugging from within, it arises from the application of pressure from without. Thus, for example, transient jaundice is met with as the result of closure of the common bile-duct, by pressure exerted upon it by the pregnant uterus, or by impacted fæces in the transverse colon. Certain permanent abdominal tumours may also lead to the same result, but these will with greater propriety be considered under the next head.

#### PERMANENT JAUNDICE FROM OBSTRUCTION.

In order to give as clear a view as possible of the pathology of permanent jaundice from obstruction, it will be necessary for me to give the history of a case of closure of the outlet of the common bile-duct in consequence of organic disease—such, for example, as cancer of the head of the pancreas. A case of this kind has the further advantage of at the same time furnishing us with a typical example of jaundice arising from the re-absorption of the secreted, but retained bile.

When cancer of the head of the pancreas involves the orifice of the common bile-duct, as the tumour grows, the duct slowly, and gradually becomes impervious to the passage of bile into the



intestines, until at length the flow is completely arrested. As this gradual process of occlusion of the outlet goes on, the duct itself becomes more and more distended by the retained bile, till it at length attains an enormous size. The gall-bladder being equally prevented from emptying itself, likewise becomes stretched and dilated, until it may at last become not only palpable to the touch, but even apparent to the eye through the abdominal walls. This was the case in the patient whose liver, and occluded ducts are represented in Plate I.

The distention of the bile-ducts is not limited to those situated external to the liver, but also affects those in the substance of the organ; and to such an extent may this be the case, that, on making a section of a liver that has long had its common duct obstructed, a number of large excavations are observed all over its surface, which excavations are nothing more than the open mouths of the transverse sections of the dilated ducts. Such a state of matters is tolerably well represented in the section of the liver in Plate I. Further, the effect of this obstruction to the exit, and consequent accumulation of the biliary secretion, is not confined to the mere distention of the ducts, but causes various changes to occur in the parenchyma of the liver itself. The first of these is an increase



in the size of the organ, arising partly from the accumulation of the bile, and partly from the congestion caused by the pressure exerted on the vessels by the distended ducts. In the second place, gradually as the state of matters here described progresses, the parenchyma of the organ becomes itself affected, partly from the direct pressure exercised upon it, and partly from the derangement of its nutrition, produced by the interruption to the hepatic circulation; so that, after a time, the enlarged liver slowly, and by degrees diminishes, until it at length regains its natural size, thereby rendering, at this period of the disease, the diagnosis of the case extremely difficult. This state of matters is not, however, of long duration; for, in consequence of the continued compression of the blood-vessels and parenchyma, the nutrition of the liver is so disordered, as to lead to a gradual shrinking of the entire substance, or, in other words, to a general atrophy of the organ.

It is thus seen how in *permanent occlusion* of the common gall-duct the liver may be found *hyper-trophied* in the *first*, of *normal dimensions* in the *second*, and *atrophied* in the *third* and *last stage* of the disease.

In cases of the kind here described, it is not at all unlikely that the enlargement of the liver in the earlier, as well as its atrophy in the later



stages of obstruction, may be mistaken for the cause of the jaundice, instead of the result of the arrest of the flow of bile, and thereby lead to a grave error in treatment. The history of the case, together with a knowledge of the above facts, will, however, tend to facilitate the diagnosis. Thus, it must be ascertained :—

Firstly,—If the jaundice preceded the alteration in size of the organ.

Secondly,—If there is an absence of any history of hepatitis; and,

Thirdly,—If there is no evidence of any pulmonary or cardiac mischief likely to lead to passive congestion of the hepatic tissue.

Even with a knowledge of all these facts, however, it often baffles the skill, and acumen of the ablest physicians to discover the cause of jaundice. Every now and then cases are met with, where the patient tells us that the jaundice has gradually come on without any assignable cause, and where, after the most careful examination of his history, as well as of his physical condition, we fail to detect a clue to the diagnosis. Cases of this kind are far from uncommon, and this is the more to be regretted, seeing that unless we have a clear appreciation of the cause, it is not only difficult, but even dangerous to treat the symptom. The injudicious administration of



a remedy here, may hasten the termination we most desire to retard. The truth of this remark will, however, be better appreciated when I come to consider the rationale of the treatment of jaundice. Meanwhile, it may be advisable to point out a method capable of yielding most important information, when all the ordinary means of diagnosis fail. I allude to the chemistry of the excretions. Although the pathological chemistry of the excretions is as yet in its infancy, it has already given the scientific physician a key to the detection of several diseases, and I trust to be able to show, that even in the obscure cases of jaundice above alluded to, it not only gives us a clue to their cause, but presents us with a guide to their treatment.

In jaundice arising from obstruction, the pipe-clay stools are, as in the case of jaundice from suppression, entirely due to the absence of bile from the intestinal canal. The yellowness of the skin is in like manner caused by the accumulation of the bile pigment in the blood, from whence it exudes, and stains the tissues; and, lastly, the saffron-coloured urine results in a similar way from the elimination of the pigment from the blood by the kidneys. Instead, however, of these three conditions arising, as in the case of jaundice from suppression, from the arrest of the biliary functions



allowing certain of the constituents of the bile to accumulate in the circulation, they are, in the first place, the result of the re-absorption of the secreted bile from the distended ducts, and gall-bladder. So that while in jaundice from suppression, only those biliary products which exist pre-formed in the blood accumulate in the circulation, in cases of jaundice from obstruction, the biliary products which are manufactured in the liver, equally with those which are pre-formed in the blood, find their way back into the circulation, to be from thence eliminated with the excretions. If then, we could ascertain the presence or absence of these products in the excretions, we should be enabled to distinguish between jaundice resulting from suppression, and jaundice arising from obstruction. Let us now see what the chemistry of the excretions teaches us ; and to begin, we shall take the intestinal excretion.

#### ANALYSIS OF THE INTESTINAL EXCRETION AS AN AID TO THE DIAGNOSIS OF OBSCURE CASES OF JAUNDICE.

The intestinal excretion, in the natural state, consists, firstly,—of those portions of our food which have resisted the action of the digestive juices ; secondly,—of the excess of the modified food remaining unabsorbed ; and, thirdly,—of the excess,



as well as of the effete portions of the digestive secretions themselves. Consequently, if from any cause the digestive secretions do not act properly, the evacuation immediately becomes abnormal, and we can discover by analysis which of the secretions is at fault. Thus, for example, we know that the saliva acts upon the starchy matters of our food, the gastric juice on the albuminous, the pancreatic on the fatty, and that the biliary secretion so modifies the chyme as to allow of its rapid absorption by the lacteal, and portal vessels. If then, from any cause the elaboration, or excretion of any of these digestive juices be interfered with, more of the particular kind or kinds of food on which it acts, passes unchanged through the intestines. Thus, if the salivary secretion be affected, an unusual amount of unmodified starch is found in the stool. If the gastric juice is defective, more albumen than is normal passes away unchanged, and so on with the others.

It is clear then, that an examination of the stools must afford us important information regarding the presence, or absence of the normal secretions. A simple inspection of the stool will sometimes at once tell us whether or not bile is present. If it be present, the stool varies from a pale yellow, to a dark olive-green hue, according to the kind, and quantity of biliary colouring matter present, and



the nature of the food. It must not be forgotten however, that unless care be taken, the colour deducible from highly-coloured food may be mistaken for an excess of bile. This remark is still more applicable to medicines, for mercury, bismuth, iron, and some other mineral remedies, give rise to dark evacuations so closely resembling bilious stools in appearance, that the only way to distinguish them, is by chemical analysis; when, the presence of the mineral, together with the absence of the bile pigment, and the biliary acids (which are always to be found in normal evacuations), will at once reveal the true nature of the case. I have seen a mistake of this kind happen, and that too, where a patient labouring under jaundice from obstruction, was thought to be passing the usual amount of bile in his stools, when in reality not a particle of bile pigment was present. The colour was in this case entirely due to the food, and ferruginous remedies. Blood from the stomach or bowels, is also apt to be mistaken for biliary matter, more especially when acted on by the gastric juice, which has the property of turning red blood brown. With these exceptions, the absence of bile from the stool, is usually very easily ascertained. For if the patient be taking no highly-coloured food, or any of the medicines above indicated, the stools are of a



dirty pipe-clay colour. This is not due to the presence of any new or foreign matter, but solely to the absence of bile pigment. In these cases the evacuations, besides being white, are usually of a most offensive odour, for, among other things, bile checks intestinal putrefaction, and the development of offensive gases.

In addition to the colour, and odour of the fæces, in cases of jaundice, another important indication is to be found in the presence of fat. The presence of fat in the stools was at one time looked upon as evidence of pancreatic, at another time of hepatic disease; now, however, experimental physiology has taught us, that it in some measure depends upon both. For while, on the one hand, the pancreatic secretion emulsions the fatty part of our diet, and thereby renders it capable of absorption, recent researches, as has been already pointed out, have established the fact that the biliary secretion also plays an important part in the absorption of the oleaginous constituents of our food. Bidder and Schmidt, as was before said, have shown that a dog, after ligature of the gall-duct, absorbs less than half the average normal quantity of fat; and by experiment it has been found that this arises from the circumstance that bile emulsions only the acid fats, while pancreatic juice transforms the neutral as well as the acid



oleaginous matters. The presence of fat in the stools may be due, therefore, partly to hepatic, partly to pancreatic derangement; and I shall immediately point out how we can turn this fact to account in diagnosis, and discover in cases of jaundice from obstruction, whether the seat of the obstruction be at the outlet or in the course of the duct.

#### EXAMINATION OF THE RENAL SECRETION.

The urine affords us important information in all cases of jaundice. In fact, an examination of it alone would in many cases enable us to discover the presence or absence of this affection.

#### *Diagnostic Value of the Colour of the Urine.*

The urine of jaundice has invariably a peculiar tint, ranging from a saffron-yellow to a dark olive-green, or almost black hue. It must not be forgotten that the colour of normal urine varies with the degree of concentration. Where little is passed, being of a high, where much is passed, of a pale colour; the depth of colour depending on the degree of dilution of the urohæmatine. Again, it must also be remembered that there are many diseases, which change the colour of urine very materially, some only deepening, others actually changing the tint. Foods, and medicines also,



Plate II.

G. H. Ford.

Kidney from a Case of Permanent Jaundice.

W. West imp.





has another advantage, for if we take a measured quantity of urine, and collect, dry, and weigh the uric acid obtained from it, we can readily calculate the total quantity passed in the twenty-four hours, and thereby assist in diagnosing the presence or absence of malignant disease of the liver, as I shall afterwards have occasion to point out.

The urine of jaundice is generally described as being of a saffron colour; but if I may be allowed to form an opinion from my own observations, which are tolerably numerous, I should say that it, in colour, much more frequently resembles old ale than anything else with which I am acquainted. On standing, the colour changes very considerably, in consequence of the pigment becoming slowly oxidized by its exposure to the air. When there is a very great excess of bile pigment present in the blood, the kidneys have some difficulty in eliminating it. Occasionally even, it chokes up the renal capillaries, and thereby complicates the jaundice by inducing secondary disease in the kidney. In such cases the external surface of the kidney, after the removal of the capsule, looks as if it had been sprinkled over with ink. The black specks vary in size from the minutest visible point to that of a pin-head. The accompanying chromo-lithograph (Plate II.) represents a kidney in this condition.



It will also be observed that it is studded over with a number of small abscesses ; but whether these resulted from the blocking-up of the capillaries just alluded to or not, it is impossible to say. In the case in question no albumen was detected in the urine during life, and it was only on careful analysis, after the post-mortem had revealed the above state of matters, that a small quantity was discovered ; and even then, had not the experiment been carefully performed, the presence of albumen might have been overlooked.

*Diagnostic Value of the presence of the Bile-Acids in the Urine.*

All acquainted with the recent literature of jaundice know how hard a battle is being fought between two sets of observers in Germany, regarding the presence of bile-acids in urine. One class, with Frerichs and Städler at their head, believe that the biliary acids are decomposed in the blood, and are consequently never to be detected in the urine. The other class, headed by Kühne, state as positively that they have detected these substances in the urine. Indeed, Kühne states that by adopting Hoppe's method,\* he never fails to

\* Professor Hoppe tests for bile-acids in the following manner :—The urine is boiled with an excess of milk of lime for about half an hour, and filtered to free it from the precipitate thus



detect the presence of the biliary acids in the urine of patients labouring under icterus, as well as in the urine of dogs with the bile-duct ligatured. When first studying this question, I was very much perplexed by these contradictory statements, for neither the judgment, nor the power of observation of either of the authorities could for a moment be called in question; and on experimenting for myself, so unsatisfactory were the results obtained, that I almost threw the question aside in despair. On one occasion, however, I at length met with such unmistakeable evidence of the presence of bile-acids in the urine, that I could no longer doubt the fact of their existence, and was forced to search for an explanation of the previous contradictory results. Fortunately, it was not very long before a solution to the difficulty was obtained, and, what was of still greater importance, led to the observation that the contradictory results arose from a circumstance which might be turned to account, as a means of differential diagnosis. The discovery was, that in certain cases of jaundice not a trace of the biliary acids is to be detected in the urine, although the

formed. The filtrate is evaporated to dryness, decomposed with hydrochloric acid, washed with water, and then extracted with alcohol. The alcoholic extract contains the bile-acids, which are recognised by Pettenkofer's test.



bile pigment is present in abundance; while in certain other cases both biliary acids, and bile pigment occur in notable quantity. What, then, is the cause of this difference? Simply this. In jaundice from suppression the liver does not secrete bile; consequently no bile-acids being formed, none can enter the circulation, and they are therefore not to be detected in the urine. In jaundice from obstruction, on the other hand, bile is secreted, and absorbed into the blood; and the bile-acids not being all transformed in the circulation, as Frerichs supposed, are eliminated by the kidneys, and appear in the urine, where they can be detected by Hoppe's method, or even, with proper precautions, by simply adding sulphuric acid and sugar. Here, however, some skill and experience are requisite, in order not to confound the colour produced by the action of the reagents on other substances with the fine purple produced by the biliary acids. As the majority of cases of jaundice result from suppression of the hepatic function, and as many of the cases of obstruction ultimately merge into the former, it is easily understood how the existence of the biliary acids in the urine has been so frequently denied. I have myself seen, in a case of obstruction of the common duct, the biliary acids slowly and gradually diminished in the urine, until they at length almost entirely dis-



appeared as the case approached a fatal termination. Here the disappearance of the biliary acids went on step for step with the impairment of the secreting powers of the liver, in consequence of the pressure exercised on its parenchyma by the retained bile.

The readiest mode by which the biliary acids may be detected is the following: To a couple of drachms of the suspected urine add a small fragment of loaf-sugar, and afterwards pour slowly into the test-tube about a drachm of strong sulphuric acid. This should be done so as not to mix the two liquids. If biliary acids be present, there will be observed at the line of contact of the acid, and urine—after standing for a few minutes—a deep purple hue.\* This result may be taken as a sure indication that the jaundice is due to obstructed bile-ducts. On the other hand, the absence of this phenomenon, and the occurrence of merely a *brown* instead of a *purple* tint, although, in the earlier stages of jaundice, equally indicative of suppression, is of course, for the reasons already given, no indication of the cause of the suppression. That must be gleaned from other circumstances.

It is seen that I have taken no notice of

\* The immediate formation of a reddish coloured line is due to the acid setting free urohæmatine, the normal colouring matter of the urine.



Frerichs' theory regarding the bile-acids being changed into bile pigment. I have done so advisedly, feeling as I do, that when that observer investigates the subject more fully, he will himself abandon such an untenable doctrine, founded as it is, on an erroneous view regarding the nature of bile pigment. The colour induced by sulphuric acid on the acids of the bile, is as different in its chemical nature from animal pigment, as any two substances can possibly be. Indeed, they have no bond of connection whatever, except the mere tint. All animal pigments, whether they be green, like bile-colouring matter, or red, like hæmatine, spring from the same source, and contain iron. Besides this, the mere fact of an increase of animal pigment being found in the urine after the bile-acids have been injected into the circulation, to which Frerichs attaches such importance, in reality proves nothing more, as Kühne pointed out, than that an increased destruction of blood corpuscles has taken place. I have found the urine of dogs loaded with dark colouring matter after injecting chloroform, and other stimulants into their portal veins, in order to establish artificial diabetes; and, assuredly, in these cases the presence or absence of bile-acids in the blood had nothing to do with the result.

*Diagnostic Value of the presence of Tyrosine, and  
Leucine in Urine.*

There are two other abnormal products occasionally met with in the urine of jaundice, namely, tyrosine, and leucine. These substances, although for many years known to chemists, attracted comparatively little attention until Frerichs discovered their diagnostic value in hepatic disease.

FIG. 4.

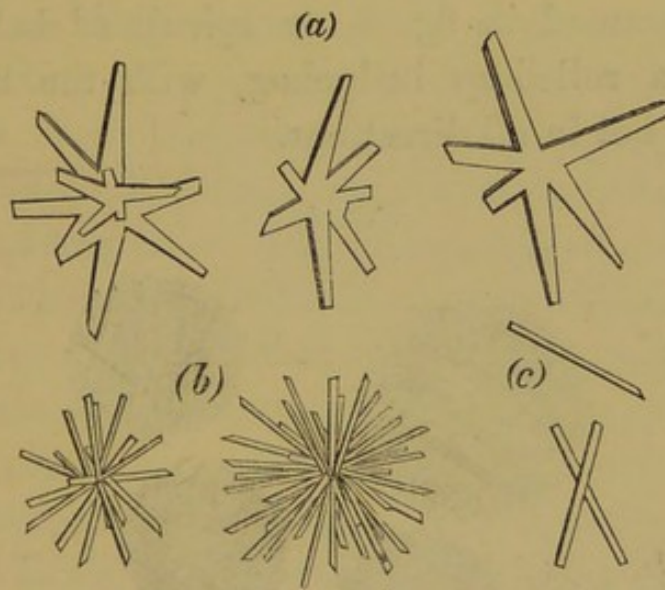


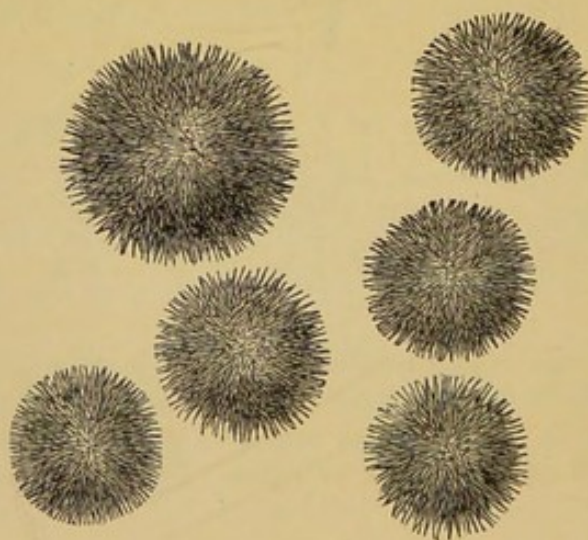
Fig. 4.—Crystals of pure tyrosine, obtained from the urine of a case of chronic atrophy of the liver, following upon obstruction of the bile-duct. (a) Large crystals. (b) The more common form of the stellate groups of needle-shaped crystals. (c) A few separate fragments of needle-shaped crystals.

In that peculiar form of complaint, described as acute or yellow atrophy of the liver, the



urine is said invariably to contain tyrosine, and leucine. The presence of these substances may therefore assist us in diagnosing the case. When tyrosine, and leucine are present in quantity, they are very readily detected, all that is required being slowly to evaporate an ounce of urine, to the consistency of syrup, put it aside during a few hours to crystallize, and then examine it with the microscope. The tyrosine is recognised by being in fine stellate groups of needle-like crystals, as represented in fig. 4, or spiculated balls not unlike a rolled-up hedgehog, with the bristles sticking out in all directions.

FIG. 5.



Spiculated balls of tyrosine, from the urine of a case of acute atrophy of the liver. When these were re-dissolved, purified, and re-crystallized, they assumed the form represented in Fig. 4 (*b*).



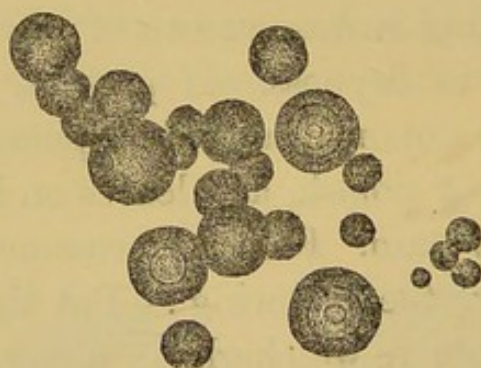
Tyrosine may be obtained in a pure state by adding to four ounces of urine a solution of acetate of lead, till a precipitate ceases to form, filtering, and freeing the liquid from the excess of lead by a current of sulphuretted hydrogen, again filtering, and evaporating the clear solution. The tyrosine is now colourless, and crystallizes with the microscopic characters above alluded to, but still better marked. Tyrosine may be further recognised by putting a few crystals on a platinum spatula, adding a drop or two of nitric acid, and evaporating to dryness. If present, the yellow residue thus obtained assumes a pumpkin hue on the addition of potash, and leaves on incineration a dark greasy stain. Frerichs recommends another test, namely, the following:—Put the suspected substance into a watch-glass, along with some sulphuric acid, and after they have been in contact about half an hour, dilute the mixture with water. Next boil, and then neutralize with carbonate of lime. Filter, and to the clean filtrate add a few drops of perchloride of iron, devoid of free acid. The formation of a dark violet blue colour indicates the presence of tyrosine.

Leucine is known by its flat, circular, oily-looking discs, without any crystalline structure. At the first glance, a globule of leucine might be mistaken for oil, not only on account of its micro-



scopical characters, but also on account of its being lighter than water. The globules of leucine are distinguished from those of oil by their being soluble in water, and boiling alcohol, and insoluble in ether. Besides this, the discs are occasionally opaque and laminated like the granules of potato starch. They are then not at all unlike microscopic crystals of the carbonate of lime; but the carbonate of lime crystals sink in water.

FIG. 6.



Dark globules of leucine of various sizes, resembling in appearance globules of carbonate of lime.

Both tyrosine, and leucine are usually deeply impregnated with the colouring matter of the urine.

Since Frerichs' views were first published I have found tyrosine, and leucine in the urine of cases of chronic, as well as of acute atrophy of the liver. Their presence may therefore aid in diagnosing the latter as well as the former condition of the hepatic organ.



I have little doubt that future research will discover other conditions of the liver, besides those just mentioned, in which tyrosine, and leucine, may appear in the urine; for, as will be subsequently pointed out at page 96, I have been successful in producing them artificially in the urine of animals in which there was no evidence either of acute or chronic atrophy of the liver having taken place. In the cases cited, indeed, it will be seen that the jaundice was the result of suppression, consequent upon congestion of the liver, produced by blood poisoning.

It may be added that since these observations were made I have found in the artificially concentrated urine of a case of jaundice from obstruction consequent upon impacted gall-stone, a few balls closely resembling leucine in shape, and size, but differing from it in being excessively dark in colour. No tyrosine crystals were observed, and unfortunately there was not sufficient of the leucine-like substance present in the urine to admit of its being chemically tested. I have thought it my duty to record this fact for the benefit of other observers, as there can be little doubt that we are gradually verging towards some important discovery in a diagnostic point of view.



*Melanine in the Urine.*

Four years ago (1858), Dr. Eiselt of Prague called attention to the fact that in cases of melanotic cancer of the liver, melanine appears in the renal secretion.\* When the urine is passed it is usually quite clear; but after standing it becomes of a dark colour, even as dark as porter, without, however, losing its transparency. This deepening of the colour is no doubt due to the oxidation of the melanotic pigment, as the employment of an oxidizing agent, such as nitric or chromic acid, causes the same change to occur instantly.

In addition to the cases related by Dr. Eiselt, I am able to add one of considerable importance, as it not only offers a striking illustration of the correctness of his views, but has the double advantage of being an unbiassed record of facts, in consequence of its having been observed, and recorded long before Dr. Eiselt's views were published, and therefore at a time when the author had no idea of its significance. The case occurred about thirteen years ago, in the wards of the Royal Infirmary of Edinburgh. The history of the case I extract from my private note-book. It is briefly as

\* Dr. Eiselt states that he also found melanine in the urine in a case of melanotic cancer of the eyeball.



follows:—In the month of May a sailor was admitted into the clinical wards of the Royal Infirmary with symptoms of jaundice from enlarged liver. He stated that he had been a great deal abroad, in hot climates, and admitted that he had been a hard drinker. On admission his skin was of a dusky yellow colour, and had been so since the month of February. The liver was considerably enlarged, and he complained of sudden violent pains in the neighbourhood of the umbilicus. The pain was usually most severe during the night. The urine was of a dark colour, and on the addition of nitric acid, became nearly quite black. It contained no albumen. The patient died ten days after admission. On post-mortem examination, the hepatic duct was found blocked up with malignant deposit, and the liver of a dark green colour. There was also a considerable amount of malignant deposit in the mesentery. This patient, as frequently happens in such cases, became delirious before death.

In jaundice arising from melanotic cancer of the liver, the recognition of the presence of melanine in the urine would be an important aid to the diagnosis. Care must be taken not to confound the dark olive-green urine occasionally met with in other forms of jaundice, with the melanotic urine just described, or both



patient and doctor may become unnecessarily alarmed.\*

*Urea, Uric Acid, and Sugar.*

The presence, and quantity of certain other substances met with in the urine of jaundice, although not peculiar to that condition, nevertheless afford us important information, not only as to its cause, but also as to its probable mode of termination.

Firstly, a correct knowledge of the quantity of urea, and of uric acid passed in the twenty-four hours is of great value; and, secondly, the presence, or absence of sugar is a fact which ought never to be lost sight of. The value of this statement, as well as of several of the preceding, will, I think, be better appreciated by giving a short account of a case of obscure disease (where a correct diagnosis, and prognosis could not have been arrived at without the application of the chemical knowledge referred to), than by any mere abstract

\* While I was Resident Physician in the Royal Infirmary of Edinburgh, in 1850, a woman, aged 28, was admitted with a universal and bright jaundice of three weeks' standing. Her urine was high coloured, and of a specific gravity of 1022. It contained a small quantity of albumen, and became perfectly black on being boiled with nitric acid. In this case there was no reason to suspect malignant disease of the liver; the colour of the urine was, therefore, most probably due to the bile pigment being more than usually oxidized. After a six weeks' stay in the hospital, I dismissed the patient as cured.



treatment of the question. I shall, therefore, at once proceed to relate the brief history of the case.

A gentleman, aged fifty, who had been a remarkably healthy man, observed, within eighteen months of his death, that his skin gradually assumed a more and more jaundiced tint without any assignable cause. The stools were clay-coloured, the urine loaded with bile pigment. Soon afterwards, the patient began to lose flesh. The liver became enlarged, and somewhat tender to the touch; the gall-bladder being at the same time so distended that it could be seen, as well as felt, projecting from under the false ribs. As the case resisted the usual remedies, the patient was recommended to try change of air. During his absence from town, he suddenly passed a large quantity of yellow matter by stool (supposed to be bile), and immediately afterwards the fulness in the abdomen disappeared. On the patient's return to town, the gall-bladder could no longer be seen or felt, and it was naturally supposed that it had emptied itself on the occasion referred to. As, notwithstanding this, the jaundice continued, and the health and strength gradually declined, Dr. Prance, under whose care the patient was, sought the assistance of a physician of distinguished reputation in these affections. At this period, how-



ever, the entire absence of physical signs beyond the clay-coloured stools, and those directly referable to the jaundice, rendered it impossible for any decided opinion to be arrived at. The liver had now resumed its natural size, and the only thing detectable was slight tenderness on pressure, with a doubtful fulness in the pancreatic region. These signs, associated as they were with gradually increasing emaciation and debility, led to the suspicion of malignant disease, either in the course of the bile-ducts, or at the head of the pancreas. About this time it was discovered that the patient occasionally passed a considerable amount of a fatty-looking matter by stool—not mixed with the motion, but separate, though upon it. After the passage of this matter, there in general appeared to be a slight improvement in the patient's condition. The substance in question, on cooling, solidified into a firm pale-brown matter, resembling Windsor soap, and not at all unlike some of the biliary products. This led to the idea that it might be composed of the fatty acids of the bile. On one occasion a portion of it was forwarded to me for analysis, and on subjecting it to chemical examination it proved to be, strangely modified fish-oil, the oleine of which had entirely disappeared. In fact, it was nothing but the sparingly soluble fatty acids of cod-liver oil, which had



been transformed in the stomach, and from which all the liquid principles had been absorbed. This was considered an important discovery, as it not only negatived the idea of the bile still reaching the intestines, but also proved that the *pancreas*, as well as the *liver*, was affected. Having thus learned that the pancreatic juice, as well as the bile, failed to reach the intestines, an effort was made to counteract the pernicious effect on the system caused by the absence of the former secretion, by giving  $1\frac{1}{2}$  grains of pancreatine in the form of pill three times a day. During the period that the patient was taking this medicine, the quantity of fat passed by stool was supposed to diminish. No decided improvement in the patient's condition took place, however, and on the 2nd of November the gentleman was brought to me by his medical attendant. At this time the patient was much in the state already described,\* and after a careful physical examination, I failed to elicit any new fact of importance. The hepatic dulness was perfectly natural; there was no tenderness to speak of, no history of gall-stones, and

\* I noted his state to be as follows:—Skin of a black jaundiced tint (dark green). Eyes deeply stained. Lips anæmic. Considerable emaciation and debility. Extreme languor. Appetite good. Tongue, and pulse not remarkable. Slight pain on pressure over the gall-bladder. Indistinct fulness in pancreatic region, and to the left of middle line.



no evidence of any tumour beyond the doubtful fulness in the pancreatic region. The digestive, and other functions of the body, except those already mentioned, seemed unimpaired, and yet the patient's strength daily declined. As physical as well as symptomatical diagnosis proved inadequate to unravel the mystery of this obscure case, and as chemical means had already, in as far as it had been tried, been of advantage, it was resolved to subject the excretions to a rigid chemical examination. The patient was accordingly desired to collect all the urine he passed during twenty-four hours, and while I analysed it, Dr. Prance examined the stools, in order to ascertain their composition—especially as regarded the amount of fatty and albuminous matters contained in them. The urine yielded on analysis the following result:—

## 24 HOURS' URINE.

Quantity (55 oz.)	.	.	.	1705. c c.
Re-action	.	.	.	Acid.
Specific gravity	.	.	.	1018.
Colour	.	.	.	Greenish yellow.
Urea	.	.	.	27·28 grammes.
Uric acid (crystals large, and of a dark-green colour)	.	.	.	0·511. „
Bile acids*	.	.	.	Abundant.

\* On the addition of sulphuric acid, and white sugar to the urine, a very marked, and beautiful purple hue was obtained.



Bile pigment*	.	.	.	.	Abundant.
Albumen	.	.	.	.	None.
Sugar	.	.	.	.	None.

The facts here elicited were interpreted as follows:—

1st,—The quantity of urea which might be said to be normal, was considered a favourable sign, as it indicated that the stomachal digestion was unimpaired.

2nd,—The quantity of uric acid being below the average, was likewise regarded as favourable, tending as it did to negative the idea of cancerous disease of the liver; the uric acid being in such cases usually increased.

3rdly, and lastly, the presence of the biliary acids, as well as the bile pigment, in the urine, showed that bile was still being secreted, but re-absorbed, and this led at once to the diagnosis that the case was one of jaundice from obstruction.

Here, then, was an important step gained. The next point was, if possible, to ascertain the cause of the obstruction. Taking into account the absence of any tumour, and any history of gall-stones, together with the fact of the sudden disappearance of the enlarged gall-bladder, my

\* Nitric acid at first turned the urine green, but on the application of heat it became red, and after prolonged boiling, of a pale straw colour. Hydrochloric acid changed the colour of the urine immediately to a deep olive-green tint.



first idea was that it might be a case of hydatids blocking up the common gall-duct, and that on one occasion, some large cyst had ruptured, and discharged itself through the intestines. On talking the case over with Dr. Prance, however, that idea was abandoned, and we were forced to content ourselves with the simple fact that the case was one of jaundice from obstruction of the common bile-duct, complicated with occlusion of the pancreatic duct, which fact had been previously ascertained by the discovery of the fatty acids in the fæces. About this time the patient took three grains of benzoic acid, in the form of pill thrice a day, and it was thought, with the advantage of slightly diminishing the jaundiced state of the skin. But no permanent benefit was obtained, and after a time this remedial agent had to be discontinued, in consequence of its having induced slight dyspepsia. In the letter I received informing me of this fact, it was also noted that there was much less both of the oily matter, and albumen in the stools. There was, at the same time, a considerable deposit of urates in the urine. The specific gravity continued to be about 1018. The quantity in twenty-four hours about forty ounces. On the 29th of November, the patient was again brought to me, and we made a careful examination of the size, shape, and exact position of the



hepatic organ. The measurements were found to be 5 inches at the extreme right, 4 inches at a line drawn perpendicularly to the nipple, and  $2\frac{3}{4}$  inches midway between nipple and sternum. Beyond the centre of the sternum the liver did not reach. As regards the size of the liver then, there was still nothing very remarkable.

On this occasion it was observed, that the patient's memory was not so good as formerly, and that there was a certain amount of mental as well as bodily languor. His hearing was likewise sluggish, the words having occasionally to be repeated before they made an impression on the cerebral organ. This, no doubt, arose from the poisonous effects of the bile circulating in his blood.

It may be here mentioned, that in cases of jaundice from suppression we seldom or never meet with those extreme symptoms of cerebral disturbance which are so common in cases of jaundice from obstruction. I believe the reason of this difference in the two forms of jaundice arises from the circumstance that the really poisonous parts of the bile are the biliary acids, and that they, like urea, are powerful narcotic poisons. The results of the experiments on artificial jaundice (page 95) led me to this conclusion.

As neither the symptoms nor physical signs threw any additional light on this interesting case,



it was determined once more to bring chemistry and the microscope to bear upon it, with the view of, if possible, extending the information these methods of investigation had already yielded. Accordingly, a specimen of the urine was again obtained for analysis, and it yielded the following results:—

## 24 HOURS' URINE.

Quantity, (43 oz.) . . . . .	1333 c. c.
Specific gravity . . . . .	1016
Reaction . . . . .	Acid.
Urea . . . . .	23·994 grammes.
Uric acid . . . . .	0·266 „
Bile pigment . . . . .	Abundant.
Bile acids . . . . .	{ Small quantity.
Sugar . . . . .	A little.
Solids (total) . . . . .	41·989
Organic matter . . . . .	31·992
Inorganic . . . . .	9·997

A marked change is here seen to have occurred in the constitution of the renal secretion. First—the quantity of urea has notably diminished (from 27·28 to 23·99 grammes, or in other words, from 423·84 to 370 grains.) The amount of uric acid has also fallen (from 0·511 to 0·266 grammes, or in other words, from 8 to 4 grains); while at the same time the biliary acids have considerably decreased. These changes are also seen to be accompanied by another, which I at once regarded

as a most unfavourable sign,—namely, the appearance of sugar in the urine. Although the quantity of sugar was as yet small, and it was associated with a diminution in the bile acids, it nevertheless made me look forward with gloomy forebodings, for as far as my experience goes, when the urine becomes saccharine in the course of a chronic, and exhausting disease, it has generally been the forerunner of a fatal termination. This case, I am sorry to say, proved no exception to the rule. There was, indeed, but one consolatory fact in the analysis, and that was the diminution of the uric acid, which, as I before remarked, tended to negative the idea of malignant disease of the liver, and this was a great source of satisfaction to the patient.

Eight days later, 12th November, a qualitative, and quantative analysis of the urine was again made, with the following result:—

## 24 HOURS' URINE.

Quantity (33 oz.)	.	.	.	.	1023 c. c.
Reaction	.	.	.	.	Acid.
Specific gravity	.	.	.	.	1017
Urea	.	.	.	.	15·345 grammes.
Uric acid	.	.	.	.	?
Bile acids	.	.	.	.	None.
Bile pigment	.	.	.	.	Abundant.
Sugar	.	.	.	.	Increased.



Tyrosine, and leucine*	.	.	.	In small quantity.
Solids (total)	.		23·426	
Organic matter	.	.	.	17·698
Inorganic	.	.	.	5·728

Here, is now to be observed, the rapid downward progress of the case. Stomachal digestion, as indicated by the amount of urea, is much impaired. The general health, as indicated by the sugar, is sadly affected, and, to crown all, tyrosine, and leucine, the indicators of atrophy of the liver, have made their appearance. So unfavourable was the result of this analysis considered, that Dr. Prance felt himself bound to fulfil a promise he had made to the family some time previously, of warning them of approaching danger, when we had no longer any hope of the patient's recovery.

Some time afterwards, in the beginning of December, we again saw the patient together, and made a physical examination of the hepatic organ, the result of which only confirmed our suspicions. The liver was decidedly smaller. The epigastric tenderness was increased. The

\* On precipitating the urine with the acetate of lead, filtering, and freeing the clear liquid from the excess of that reagent by means of sulphuretted hydrogen, and again filtering, the liquid, on evaporation, was found to deposit small crystals of tyrosine, and to have floating in it, and on its surface, round balls of leucine.



jaundiced tint deeper. Petechial spots had now appeared on the trunk, and arms. The lower extremities were œdematous, and the abdomen two-thirds filled with fluid.

On the 31st December, I received a sample of urine, and a note saying that the patient had slightly rallied. But on examining the urine, it was found to have a neutral reaction—it had previously always been acid—to be of a specific gravity of 1019, and on standing, to deposit a copious sediment of lithates, coloured intensely yellow with the bile pigment. Curiously enough, the bile-acids had reappeared; but only in quantity sufficient to admit of their being detected. In spite of these trifling changes for the better, the ominous one of an increased amount of sugar was still there.

A few days later, and just before his death, the patient had the benefit of another physician's opinion, which, although it differed somewhat from the foregoing, was, nevertheless, equally unfavourable, for he considered it a case of malignant disease.

The gentleman having noticed that his case excited considerable interest, and some difference of opinion among his medical attendants, directed that his body should be examined after death; and as this wish was seconded by his wife,

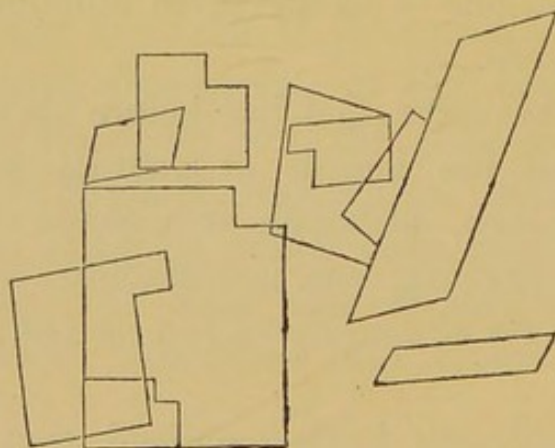


a lady of superior mind and accomplishments, a post-mortem examination was accordingly made, with the following results:—

Firstly,—The pancreatic duct, as had been suspected, was found completely occluded at its outlet, and so distended by the accumulated secretion, that it readily admitted the point of the little finger. (Vide Plate I., *g.*)

Secondly,—The orifice of the common bile-duct was in like manner completely obliterated, and the duct itself immensely distended with dark thick tarry bile, which on microscopic examination, was found loaded with beautiful crystals of cholesterine. (Fig. 7.)

FIG. 7.



The gall-bladder was enlarged to the size of a swan's egg, and contained thick tarry fluid; but no gall-stones, or masses of inspissated bile. The hepatic duct was greatly enlarged, easily admitting

the point of the finger. The cystic duct was also dilated, though in a much less degree. (Vide Plate I., *c. d. e.*)

Thirdly,—The gall-bladder, duodenum, abdominal parietes, and in fact all the abdominal viscera, were intensely stained, almost blackened, by the osmosed bile.

Fourthly,—The bile, on analysis, was found to contain in one thousand parts:—

Water . . .	694·45
Solids . . .	305·55
	<hr/>
	1000·00
	<hr/>

Pigment . .	}	Organic matter . .	288·99
Bile-acids . .			
Cholesterine . .			
Soda . . .	}	Inorganic salts. . .	16·56
Potash . . .			
Iron . . .			

Whereas a specimen of normal bile taken from the gall-bladder of a woman aged sixty-one, was of a specific gravity of 1020, and contained in 1000 parts:—

Water . . .	933·27
Solids . . .	66·73
	<hr/>
	1000·00
	<hr/>



Pigment	.	}	Organic matter	.	56.73
Bile acids	.				
Cholesterine	.				
Sugar	.				
Soda	.	}	Inorganic salts	.	10.00
Potash	.				
Iron	.				

The difference in composition of these two biles is very striking. The one contains more than four times as much solid matter as the other; and if the relative amount of organic, and inorganic substances be compared, the curious fact is observed, that the difference in the amount of solids in the two cases, is almost entirely due to the change in quantity of organic matter. The inorganic salts have not even so much as doubled themselves in the abnormal bile. Whence is this? Soda is the chief inorganic substance found in bile, and we have seen that it occurs in the form of glycocholate, and taurocholate of soda, substances which, as before remarked, are re-absorbed from the distended ducts, and gall-bladder into the circulation, from whence they are constantly being eliminated with the urine; and this, no doubt, is one of the causes why the inorganic salts are proportionally in such small quantity in the abnormal bile of jaundice from obstruction.

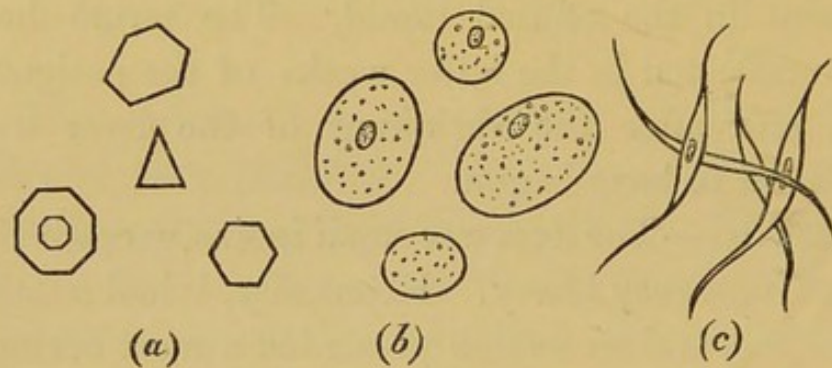
Fifthly,—In the abdomen was a considerable quantity of dark straw-coloured serum, which on the addition of strong sulphuric acid became of a fine emerald-green colour, in consequence of the presence of bile. Traces of sugar were also present in the effused liquid. The serum had only collected in the latter weeks of the patient's life, and after the shrinking of the liver was observed to have begun.

Sixthly,—The liver was small in size, excessively dense, and very heavy. Externally, it had a dark olive hue, and on section presented a most curious appearance. The section was of an almost uniform yellowish-green colour, and studded over with excavations (Plate I., *b*), from which thick bile streamed in all directions. The apparent excavations were nothing more or less than immensely distended ducts. On looking into the ducts, it was observed that they presented the appearance of possessing valves. On microscopical examination, the hepatic cells were found smaller than normal, as if partially atrophied. The nuclei were unusually well marked, in consequence of the fat granules being almost entirely absent. (Fig. 8, *b*.) In the field of the microscope were a number of caudate or spindle-shaped cells (Fig. 8, *c*.), from the epithelial lining of the ducts. In the hepatic tissue were found some beautiful



stellate crystals, as well as a number of separate needles of tyrosine. A few small crystals of cystine were also found. (Fig. 8, *a*.)

FIG. 8.



Seventhly,—The kidneys were enlarged, pale, and fatty-looking; and all over the surface of the section, as well as immediately under the capsules, which were very loosely attached, were small abscesses. The surface was also studded with numerous minute dark bile-pigment points, and it is possible that the abscesses were the result of the blocking up of the capillary vessels by the pigment deposit, as previously alluded to, page 57.

Eighthly,—The head of the pancreas was considerably enlarged, and on cutting into it, a quantity of pus oozed out from an abscess in its interior. The abscess was found to communicate with a large ulcerated spot in the duodenum. (Plate I., *f*.) On microscopical examination, the

tumour of the pancreas was found to consist of an hypertrophy of the normal gland tissue, being, in fact, a chronic inflammatory tumour of the gland substance.

In no portion of the body was a trace of cancer detected, nor any enlargement of the mesenteric or other glands, to justify even a suspicion of malignant disease. So the opinion arrived at regarding the pathology of this case is, that the disease originated in an inflammatory affection of the pancreas, during the progress of which, the openings of the bile, and pancreatic ducts became blocked up; the interruption to the excretion of the bile giving rise to the jaundice, and at the same time inducing engorgement, and enlargement of the liver. The inflammatory affection of the pancreas had probably ended in the formation of an abscess, which, pushing the enlarged liver forwards, admitted of the distended gall-bladder being seen, and felt through the abdominal parietes. At length the abscess burst, and suddenly emptied itself into the duodenum; the yellow fluid discharged from the intestines being not bile, as the patient had supposed, but pus. No sooner had the abscess emptied itself, than the liver returned to its natural position, and thus accounted for the distended gall-bladder so suddenly ceasing to be seen or felt. The ulcer in the duodenum appears



to be the mouth of the abscess, which has probably been prevented closing, partly on account of the occasional draining away of pus, which, being in small quantity, and mixed with the stools, escaped detection; and partly to the constant irritation of the passage of the food, there being no bile or pancreatic fluid to neutralize the acidity of the chyme. This might even be sufficient of itself to delay the healing process. The ultimate gradual atrophy of the liver would arise from the continued pressure of the distended bile-ducts interrupting the hepatic circulation, as formerly pointed out at page 48. Lastly, there being no bile or pancreatic juice admitted into the intestines, the greater part of the food taken passed out of the body unabsorbed, and the patient, though possessing an excellent appetite, and taking plenty of food, actually died of slow starvation.

My object in giving such prominence to this interesting case, is to show how valuable an adjunct physiological chemistry is to the other methods of diagnosis in obscure diseases of the abdominal organs, and to encourage others to follow in the same path; for it must be remembered that the foregoing was no dead-house diagnosis, but that every fact here stated was discovered and recorded before death.



Having now explained the mechanism of the two forms of jaundice—that arising from suppression, and that induced by obstruction—it only remains for me to remind my readers, that there is frequently a combination of the two conditions. Jaundice from obstruction, for example, cannot long exist without becoming complicated with jaundice from suppression. The continued backward pressure exerted on the hepatic parenchyma by the over-distended bile-tubes, sooner or later impedes the circulation in the organ to an extent sufficient to induce an impairment, if not an almost total arrest of the biliary secretion. Hence it is, that in the last stage of jaundice from obstruction, the biliary acids gradually diminish, and at last finally disappear from the urine. We have it, nevertheless, in our power to distinguish between the two forms of disease—for whereas, in jaundice arising from simple suppression, there is only an absence of the bile-acids; in jaundice from obstruction, complicated with suppression, the absence of the bile-acids is usually associated with the presence of tyrosine, and leucine. For before complete suppression occurs as a result of obstruction, the hepatic tissue has already had its nutrition so impaired, as to admit of the formation of these foreign substances. Lastly, the history of the case will of itself be an important guide.



## EPIDEMIC JAUNDICE.

It is seldom that jaundice attacks persons in an epidemic form; as it does so occasionally, however, and that too in almost all countries, it is necessary that I should say a few words on its pathology. In a quotation, in the "Medical Times and Gazette," from the "Recueil de Mémoires de Médecine Militaire," vol. iii. p. 374, it is stated that, "M. Martin gave an account of an epidemic of jaundice which he had the opportunity of observing among the artillery and engineers of the French army stationed at Pavia during the Italian war. It commenced during the great heats of August, and terminated by the end of October. There occurred 71 cases in an effective of 1022 men. The causes he considers to have been the unusual heat, which gave rise to great congestion of the liver, the fatigue of long marches (the mounted men suffering oftener in proportion than the unmounted), indulgence in alcoholic drinks, and marsh miasmata. Great increase in the size of the liver in most of the cases, and of the spleen in many, was observed, and all complained of pain in the epigastrium and in the hypochondria. In fact, this last was the first symptom of the approaching jaundice. None of the cases proved fatal. Professor San-Galli in-



formed M. Martin that a similar epidemic prevailed in the town of Pavia at the same time."

That jaundice may also occur in an epidemic form among pregnant women, has been shown by Dr. Saint-Vel, who relates that, "In 1858 the island of Martinique was, without appreciable cause, visited by an epidemic of jaundice, remarkable for its severity in pregnant women. It broke out at St. Pierre towards the middle of April, attained its maximum height in June and July, and terminated towards the end of the year. All races were attacked; the patients were mostly adults; no liver-complication could be detected; nor could any resemblance be traced between the disease and yellow fever. It was fatal to females only, especially during pregnancy. Of thirty pregnant women who were attacked at St. Pierre, ten only arrived at the full period of pregnancy without presenting any other symptoms than those of ordinary jaundice. The other twenty all had abortion or premature labour a fortnight or three weeks after the commencement of the attack, and died in a state of coma, which appeared a few hours before or after the expulsion of the foetus. The females who died were from the fourth to the eighth month advanced in pregnancy. In some cases, slight delirium preceded the coma, which was never interrupted, but became more and more



profound up to the time of death. Its longest duration, in two cases, was twenty-four and thirty-six hours. It was not preceded by any notable modification of the general sensibility, nor of the respiration or circulation. Hæmorrhage was absent, except in one case, where a female had it before delivery. When death was delayed till three or four days after delivery, the lochia were healthy. Almost all the children were still-born; some lived a few hours; one alone survived. None of the infants had the icteric colour; nor was there any sign of jaundice in the ten children born at the full term."

The foregoing translation from the "Gazette des Hôpitaux," 20th November 1862, appeared in the "British Medical Journal" of the 7th of February, 1863, p. 141.

We have it further stated in the "Lancet" of the 21st February 1863, under the head of the "Health of Rotherham," that, "scarcely had the late fatal epidemic of fever subsided ere another, less fatal, but as widely spread, took its place. In last November several persons were attacked with jaundice, and now not less than 150 persons are suffering from it. None of those who were attacked by the late fever are suffering from the present epidemic."

When we reflect on the facts here related, we



can have little difficulty in forming an opinion of the pathology of jaundice occurring in an epidemic form. Its mechanism seems to be precisely similar to that of the isolated cases of the disease which are every now and then met with as the result of blood-poisoning. I have recently seen a case of well-marked jaundice supervene on an attack of scarlet fever, and as it affords a tolerably good illustration of the pathology of such cases, it may, perhaps, be briefly given with advantage.

A London cabman, aged 23, was admitted under my care into University College Hospital, on the 2nd March of the present year. He stated that he had always enjoyed good health, but that lately he had been much out of spirits, in consequence of the death of one of his relatives. On the 25th February, after three days' illness, a scarlatinal rash appeared all over his chest, and extremities, and four days later (the day before his admission), he became jaundiced. March 3rd. His skin is now of a bright yellow colour, and when the finger is rapidly drawn across it, a pink line immediately takes the place of the yellowness, showing that there is still great subcutaneous vascularity. The throat is sore, and there is considerable difficulty in swallowing. The conjunctivæ are intensely yellow—proportionally more so than the skin, in consequence of the scarlatinal hue being still



blended with the tint of the latter. The urine is high coloured, has a slight deposit of urates; contains a large amount of bile pigment, but no bile-acids. The stools have not been observed to be clay-coloured. The liver is enlarged (dulness extends  $5\frac{1}{2}$  inches in a perpendicular direction), and tender on pressure. He complains of pain in the hepatic region on taking a deep inspiration, and of a general uneasiness at other times. Has no sickness or vomiting. The mucous membrane of the tongue is red and raw-looking; flakes of epithelial fur are readily detached from it.

The case was at once diagnosed as one of jaundice from suppression. Its mechanism being supposed to be identical to that of the cases discussed at pages 25—9 under the head of jaundice arising from active congestion of the liver induced by blood-poisoning, a dose of calomel and jalap was accordingly administered, with the view of removing the portal congestion, and with the most satisfactory result; for, notwithstanding the jaundice being complicated with scarlatina, a very decided improvement in the colour of the skin took place within twenty-four hours, the other symptoms remaining as before. March 10th. The calomel and jalap was repeated on the 4th, and since then the skin has gradually become paler. It is now scarcely tinged.



To return to the cases of epidemic jaundice; they, as I have just hinted, are due to a precisely similar cause—blood-poisoning—either the direct result of miasmata, or of contagion.

A further explanation of the reason why jaundice occurs in an epidemic form, may be found in the circumstance that in all febrile states of the general system some one or other of the internal organs is liable to become congested. For example, typhus is, as a rule, complicated with cerebral congestion, typhoid with mesenteric, ague with splenic, scarlatina with renal, and so on. It is not, however, necessary that the organs should be affected in the same relation to the disease as is here given. On the contrary, in one epidemic of typhus, the brain may be congested, in another the lungs, and in a third the liver; and so also with other fevers. Hence we can have little difficulty in understanding why epidemics of jaundice every now and then occur, seeing that they are but the secondary results of other epidemic affections, although, as occasionally happens, the jaundice is the chief, if not the only well-marked symptom.

#### ARTIFICIAL JAUNDICE.

What is the source of the tyrosine, and leucine found in the urine, in cases like those previously described? Being well aware that the physiologist



has it in his power to produce almost any pathological state or artificial disease at pleasure, I set about imitating on an animal the effects produced in the human subject by obstruction of the bile-ducts. Hitherto, artificial jaundice has been usually induced either by ligaturing the gall-ducts or injecting bile into the circulation; but as both of these methods were in the present instance objectionable—the first on account of the constitutional disturbance liable to be induced by the severity of the operation; the second from the bile being all at once thrown into the circulation, and thereby producing toxic effects, besides the danger of its too rapid elimination by the urine—I adopted another plan, which came much nearer to the state induced by disease in man—I took the bile of three healthy dogs, and injected it under the skin of a fourth. In this case the effects of the operation were almost *nil*, and the bile was at the same time placed in a position favourable for its slow absorption, just as in the human subject. During the first two days the animal remained comparatively well, the urine was normal in appearance, and contained neither bile-pigment, nor bile-acids. But on the third day the animal became ill, and on the fourth jaundice set in. He died on the fifth. After death the urine was found to contain not only bile-



pigment, and bile-acids, but also the diseased products, leucine, and tyrosine; and what was more interesting still, the urine was loaded with sugar, just as occurred in the case imitated.

It will be remembered that in speaking of the bile-acids, I mentioned that while glycocholic acid is a crystalline, taurocholic is a non-crystalline substance. Tyrosine, and leucine stand in a similar relation to each other; tyrosine being crystallizable, leucine non-crystallizable. Now, taking this fact into account, together with the fact, that when the bile-acids are allowed slowly to enter the circulation, they reappear in the urine, accompanied with tyrosine, and leucine; and also with the third fact of these latter substances being found in the liver when the biliary function is interfered with, I am inclined to look upon tyrosine, and leucine as the products either of the arrested, or of the retrograde metamorphosis of glycocholic, and taurocholic acids. Moreover, I have found in one case, after injecting bile in the way before mentioned, into the cellular tissue, crystals of tyrosine spontaneously form in the bile taken from the animal's gall-bladder after death, and merely allowed slowly to evaporate. This result strengthens the foregoing opinion.

Frerichs states that he has never detected the biliary acids in the blood, even after bile had



been injected into the circulation. In a remarkable case where 1 oz. of ox-bile killed a dog in less than five minutes from the time it began to be slowly injected into the jugular vein, I detected the bile-acids in a clear extract of the blood, with facility. This leads me to mention that, contrary to the statement of Frerichs, and in accordance with that of Kühne, the injection of the pure bile-acids into the blood is very dangerous, and that even the injection of pure bile into the cellular tissue, often proves fatal in the course of twenty-four hours, thereby showing that the constituents of the bile are highly poisonous.

In illustration of these facts I may cite the following experiments:—

Into the cellular tissue of the back of a full-grown, and healthy-looking terrier dog, I injected the bile taken from the gall-bladders of three healthy dogs, two of which had just been killed, the other had been dead a few hours. The bile was in the first two cases neutral, in the third faintly alkaline. All the biles seemed perfectly normal. They contained no crystals of any kind. Eighteen hours after the operation the animal appeared quite well, and took his food heartily. Four hours later a remarkable change took place. The dog looked dull and drowsy, and could not sustain himself on his legs; when left to himself, he



lay on his side, and made not the slightest movement. He was not only paralyzed, but even the nerves of sensation had ceased to act, for when his tail, and feet were pinched, he was quite insensible to pain. The pupils were dilated, and the body felt cold. Death occurred twenty-three hours after the operation. Urine, and fæces were passed in small quantity immediately before death. The urine was strongly alkaline, and effervesced on the addition of sulphuric acid, thereby showing that it contained alkaline carbonates. Prismatic phosphatic crystals were present in the still fresh urine.

When tested for bile-acids, only the faintest trace was obtained, after the urine had been cleared with the acetate of lead and sulphuretted hydrogen.

The tissues of the abdomen and thorax were cedematous, but, within an hour after death, had not the disagreeable odour found in animals killed by injecting pure bile-acid. (*See foot-note at p. 39.*)

This experiment was again repeated with alkaline bile. Two ounces of ox-bile of a specific gravity of 1025 were injected under the skin of a large pointer dog. In twenty-four hours the animal was dead; the sub-cutaneous tissue all round the seat of the injection, red, inflamed, and infiltrated with



blood. The urinary bladder was empty. The gall-bladder contained  $1\frac{1}{2}$  ounces of dark bile of a specific gravity of 1040. When examined with the microscope, the blood was found to contain a large excess of white corpuscles.\*

These results rather militate against the theory of the bile being re-absorbed, in an unchanged state, into the circulation, after the completion of the digestive process.

\* It has just been said that the blood contained a large amount of white blood corpuscles. This reminds me of a fact that I have omitted to mention—namely, that in a case of severe jaundice from suppression, in consequence of cirrhosis of the liver, I found that the blood possessed a very treacle-like aspect. The serum was of a dingy yellow hue, and felt somewhat sticky to the fingers. Under the microscope the blood corpuscles were found to be large, and flabby, had a great tendency to adhere together by the edges, and become flattened on the sides whenever they came in contact. Moreover, the corpuscles looked as if they had no distinct cell-wall; some, and that too, in the freshly drawn blood, gave off buds, others split into two, each half when separate looking like a distinct blood corpuscle. In fact, the blood looked more as if it had been acted upon by some powerful chemical agent than anything else. I again examined it after the death of the patient, and found it presented all the above characters in a still more marked degree. To the naked eye it had a viscid, tarry appearance.

## TREATMENT OF JAUNDICE.

After what has been said regarding the pathology of jaundice, I need scarcely remark that the treatment must vary according to the kind of disorder we have to deal with. A line of treatment found to be beneficial in one case of jaundice, might prove very hurtful in another. For, as has been shown in the foregoing pages, jaundice from suppression, and jaundice from obstruction, are, it might be said, two entirely different diseases, with only the symptoms of yellow skin, high-coloured urine, and pipe-clay stools in common. The success of our treatment will therefore depend on our powers of diagnosis.

The general principles upon which the treatment of jaundice must be founded are as follows:—

The first and great object is, of course, as in the case of every other disease, to remove, if possible, the exciting cause. When that is accomplished, we can with safety turn our attention to the removal of its effects. I need not here detail the different exciting causes which it is our duty to remove. I have indicated them elsewhere, and the mere mention of some of their names is sufficient to denote the line of treatment which ought to be adopted. Thus, for example, if it be ascer-



tained from there being symptoms of tenderness, &c., in the hepatic region, that the jaundice arises from active congestion of the liver, the first object would of course be to subdue the congestion of that organ by means of leeches, hot fomentations, saline purgatives, &c., according to the age, sex, and constitution of the patient. On the other hand, if the jaundice be the result of passive congestion of the liver, we know well that so long as the exciting cause exists elsewhere, it will be worse than futile to attempt the removal of the hepatic congestion by direct means. In such a case, therefore, if to remedy the cause is beyond our power, our object will be to concentrate our efforts on the mitigation of its effects. Thus I might go through the whole list of causes of jaundice, and point out what appears to be the most appropriate treatment of each; but I think the time of my readers and my space, will be more profitably employed, if, instead of doing so, I turn my remarks chiefly to the therapeutical action of those remedies which we are constantly employing in the treatment of jaundice. The first remedy that merits special notice is mercury.

The benefit of mercury in cases of liver disease cannot be denied; but the injudicious employment of this drug in cases of jaundice, has frequently been followed by the most disastrous results.



There was a time when mercury was administered in all cases of jaundice, irrespective of their cause; now, however, men are fortunately becoming more careful in the employment of this drug. But there is still a mistaken notion regarding the therapeutical action of mercurial preparations. It was at one time thought that they stimulated the liver to secrete bile, and now since physiology has shown that they possess no such action, many have gone to the opposite extreme, and declared, that if mercurials do not stimulate the liver to secrete bile, their benefit in hepatic disease has been a delusion; and the dark stools following upon their employment but the result of the sulphuret of mercury formed in the intestines. I take a very different view of the matter; for though believing that mercury does not directly stimulate the liver to secrete bile, I nevertheless opine that it has an important indirect effect in reinducing the biliary secretion, and thereby curing certain cases of jaundice.

The action of mercurials seems to me, to be this.—mercury is a powerful antiphlogistic—it reduces the volume of the blood by its purgative properties, and it impoverishes the blood by its direct action on the red corpuscles. It has been poetically said by Dr. Watson, that mercury can blanch the rosy cheek to the white of the lily;



and nothing is more true, for in experiments on animals, I have found the prolonged use of mercury reduce the red blood corpuscles to a minimum. From this it is easy to understand how mercury acts in inflammatory affections; and as in the majority of cases of jaundice from suppression, the stoppage of the biliary secretion is due to active congestion of the liver, mercury proves beneficial in such cases, not by stimulating the biliary secretion, but simply by removing the obstacle to its re-establishment, namely, the hepatic congestion.

As a good illustration of the correctness of this theory regarding the action of mercurials in cases of jaundice arising from congestion, I may be allowed to quote the following case, which appeared among the Hospital Reports of the "Lancet" of the 7th December, 1861. The case is headed, "Intense Congestion of the Liver, simulating an Abdominal Tumour:"—

Alex. E——, aged forty-eight, was admitted into St. Bartholomew's Hospital, under the care of Dr. Farre, on the 17th October, 1861. The patient had, it appeared, been suffering from jaundice during six weeks. He stated that the tumour in the epigastrium began about the same time as the yellowness of the skin.

On examination, a prominent swelling was no-



ticed in the epigastric region, possessing an indistinct feeling of fluctuation, but it was found to be continuous with the liver. The motions were not bilious, but were of a clay colour, and the urine looked like pure bile. Three grains of blue pill and two of Barbadoes aloes were ordered every night. By the 25th the hepatic tumour was less, and the icterus was disappearing. On November 4th the urine was clearer and full of lithates. The conjunctivæ were the only parts observed of a yellow colour.

November 11th.—Although the pills had been continued up to this date, the mouth was not sore. The urine and stools were natural, and the patient was convalescent. A few days afterwards he left the hospital.

The result of the case clearly proved not only that the swelling was from a highly congested liver, but also that the jaundice depended on this state.

In this case it is evident that the primary beneficial action of the mercury was to reduce the congested state of the hepatic organ, and no one, I think, would venture to say that this was accomplished by the power the mercury possessed of exciting the liver to secrete bile.

If, then, the above view of the therapeutical action of mercurials be correct, it is easy to understand how, in cases of jaundice from permanent



obstruction of the gall-duct, the administration of mercury or any other lowering medicine, must prove detrimental by hastening the fatal termination.

Although mercury has not, there are some substances which have, the power of exciting the flow of bile, just as there are substances which excite the flow of saliva. Among these the mineral acids, and soluble alkalies, hold the first rank. It may seem strange that acids, and alkalies, should be here placed in juxta-position; but the reason of this arrangement will immediately appear.

According to a physiological law, acid substances have the power of exciting alkaline secretions, and alkaline substances of stimulating acid secretions.

Bile being an alkaline secretion, we can therefore have no difficulty in understanding how the mineral acids act in cases of jaundice from suppression, induced, for example, by enervation. They simply stimulate the secretion of bile.

It is not so easy, however, to comprehend the action of alkalies in similar cases. My explanation of their action is as follows:—When taken after food, and when taken on an empty stomach, the action of an alkali is entirely different. After food, and during digestion, the stomach contains a



quantity of acid gastric juice, and an alkali taken then, only neutralizes the acid. On the other hand, when an alkaline substance is introduced into an empty stomach, it acts according to the general law of exciting an acid secretion; consequently, an immediate flow of gastric juice takes place. And I believe it is the excess of this acid gastric juice, which, on reaching the duodenum, stimulates the secretion, and excites the flow from the gall-bladder of the alkaline bile, just as the mineral acids do under similar circumstances. One remark further is, however, necessary. The quantity of alkali employed for the purpose of stimulating the secretion, or of exciting the flow of the already secreted bile must be small, for if much be used, the greater part of the gastric juice will be rendered useless, in consequence of its being neutralized as fast as it is secreted. It may be laid down as a general rule, that when we desire to increase the flow of bile by means of a mineral acid, the acid must be given *after food*. When, on the other hand, an alkali is selected for that purpose, the alkali must be administered *before food*.

For obvious reasons, both alkalies and acids are counter-indicated in cases of jaundice resulting from active congestion of the liver; and it is equally evident that they can be of no direct



service in jaundice arising from occlusion of the bile-duct, where our object would be rather to diminish than to increase the secretion of bile.

Alkalies, or at least some alkalies, possess certain other properties besides those to which allusion has just been made, which may be usefully turned to account in the treatment of hepatic diseases. For example, we have been long told that alkaline carbonates are valuable remedies in cases of gall-stones, in consequence of their possessing the power of dissolving biliary calculi. Now, although I am not sufficiently enthusiastic to believe that alkalies can have much effect in dissolving gall-stones when once formed, I nevertheless believe that they are of the utmost advantage in preventing and arresting their deposition. The alkali to which I give preference is the carbonate of soda, and the reason why I prefer it to the carbonate of potash, is in consequence of my believing that the advantages derived from administering alkalies in cases of incipient gall-stones are entirely due to our being able thereby to increase the amount of glycocholate, and taurocholate of soda present in the bile; both of which substances, separately or combined, retain cholesterine in a soluble form; and, as is well known, by far the greater number of biliary calculi are composed almost entirely of pure cholesterine.



The carbonate of soda has yet another advantage. It was long ago observed by Dr. Prout that gall-stones are very common in persons of a gouty, and rheumatic tendency of body, a fact which I have myself been able to confirm on several occasions, by making a quantitative analysis of the uric acid in the twenty-four hours' urine, as recommended at page 56. In such cases the carbonated alkali is of double service, for while increasing the solvent in the bile, it at the same time counteracts the uric acid diathesis. In a case of gall-stones, in a woman aged 36, where there was an almost daily deposit of fine crystalline uric acid in the urine, it was found necessary to continue the administration of ten grains of soda, with five of rhubarb, three times a-day during two months, before this tendency to lithic acid deposit was entirely overcome.

Recently I have prescribed lithia water to persons of the uric acid diathesis in whom I had reason to suspect the existence of a predisposition to gall-stones; and when it was necessary to combine it with stimulants, sherry has been the wine selected. For some further remarks on the treatment of gall-stones, see pages 114, 119, and 123.

There is a remedy to which I wish to call special attention, namely, benzoic acid. This substance was first recommended as a remedy in



jaundice by a German physician, about six years ago. Since then, I have tried it several times, and found it of benefit in jaundice arising from suppression. In those cases of obstruction, on the other hand, in which I tried it, it appeared to be anything but beneficial. I give it in the form of pill, three times a day. Dr. Green, one of my former pupils, who has just returned from India, tells me that he acted on my suggestion, and tried it in a case of well-marked jaundice, following an attack of delirium tremens; and that by the end of eight days it would have required an experienced eye to detect the tinging of the conjunctivæ.

The following may be cited as a tolerably good example of the value of benzoic acid in cases of jaundice from enervation:—

William M——, aged eleven years, labouring under an acute attack of severe jaundice, came under my care at University College Hospital on the 2nd of February. The patient appeared to be a moderately developed, and very intelligent boy. The jaundiced condition of the skin, his mother said, was first noticed on the 30th of January, only two days before he came to the hospital. It was further ascertained that, although the boy had for some length of time been subject to monthly attacks of severe headache, and bilious vomiting, he had never before suffered from



jaundice. On the present occasion he complained of headache, but it was unaccompanied either by sickness or vomiting. On examination the liver was found normal in size, and not in the least tender on pressure. The bowels were moderately open, and the stools not clay-coloured. The urine was of a deep orange tint, and the skin of a dark yellow hue. There was an abundance of bile pigment, but not a trace of bile-acids in the urine.

As the jaundice appeared to be the result of enervation, brought on by over mental exertion, the boy was ordered to be kept from school, and not allowed to read any books (his mother said he was always reading). At the same time three grains of benzoic acid were ordered to be taken thrice a-day.

9th February.—The skin was now very much paler, the yellow colour being nearly gone. The conjunctivæ were still yellow, although less so than at last visit. The urine remained unchanged in colour. He was ordered to continue the medicine.

16th February.—Skin perfectly normal in colour; if anything perhaps a shade whiter than natural. Conjunctivæ no longer yellow. Dismissed cured.

In this case no medicine whatever, except the benzoic acid, was given.

As far as my experience goes, benzoic acid



appears to be most useful in jaundice arising from enervation or from active congestion, as in the case related at page 27 ; but in cases of the latter kind it seems to be of little service until the acute symptoms have disappeared. I am still rather doubtful regarding the mode in which it acts, although one point seems clear, namely, that it hastens the reabsorption from the tissues, and elimination from the body, of the bile-pigment. It thus appears to play the part of a whitewash ; for, as one of my lady patients once graphically said, the medicine had bleached her. On one occasion I tried benzoic acid in a case of jaundice following upon an attack of ague ; but it proved of no service. Indeed, quinine, combined with mercurials, seemed in that case to be the only remedy.

There is another drug which proves of service in jaundice from suppression, namely, podophyllin, or May-apple. This remedy, which was first introduced from America, is supposed to possess both the alterative and purgative properties of mercury. As an alterative, it is given in doses varying from  $\frac{1}{8}$  to  $\frac{1}{4}$  of a grain, three times a day ; as a purgative, from  $\frac{1}{4}$  to 1 grain, as a single dose. I have given this remedy a tolerably fair trial, and although it seems to be very useful as a purgative in hepatic disease, and to increase the flow of bile, I have found it open to two objections:



firstly, its action is slow, and not always certain ; and, secondly, in delicate females it gives rise to a good deal of griping. This latter objection can, however, to a certain extent, be counteracted, by combining the remedy with hyoscyamus. On the whole, I prefer mercurials to podophyllin, and only administer the latter in slight cases of jaundice, or in those where mercurials are counter-indicated.

For example, in cases of feeble liver, where there is an insufficient secretion of bile from want of nervous power, podophyllin is decidedly of service, for in such cases mercury is of course counter-indicated. Moreover, podophyllin can be advantageously combined with vegetable tonics, and, when given along with gentian or quinine, forms an admirable hepatic stimulant in some of the cases usually denominated "torpid liver."

I cannot refrain from making a few remarks on what I consider the injudicious employment of podophyllin. Like every new remedy, it has to run the risk of falling into disfavour, in consequence of its too ardent admirers blindly prescribing it in all cases of hepatic disease ; in many of which it must of necessity prove unsuitable, if not even detrimental. In cases of jaundice, for example, podophyllin is at one, and the same time, the bane, and the antidote. The bane in *all* cases of



jaundice from obstruction, the antidote in a *few* cases of jaundice from suppression. Having already indicated the cases in which it may be administered with advantage, I shall now call attention to one of those where it cannot be employed without injury, and one in which it is, nevertheless, frequently given. The case I allude to is that of gall-stones. When once a gall-stone has formed, and is blocking up the common bile-duct, thereby causing jaundice from obstruction, it is easy enough to understand why a substance like podophyllin, which increases the biliary secretion, is to be avoided. It is not, however, so easy to understand why the remedy is equally counter-indicated, either during the formation or sojourn of a gall-stone in the gall-bladder. This, therefore, I must explain. In speaking of the mode of formation of gall-stones in the gall-bladder (page 43), I have stated that their formation is due to the deposition of the less soluble parts of the bile, either as a consequence of these ingredients being in excess, or in consequence of the solvent, whose duty it is to retain them in solution, being in reduced quantity. It follows, then, as a natural result, that the longer bile sojourns in the gall-bladder, and the thicker it becomes, the more likely are its constituents to be deposited, and increase the size of the already existing concretion,



or give origin to a new formation. It may be further added, that the greater the amount of bile secreted, the longer is it likely to remain in the gall-bladder, and the more concentrated to become; for, as is well known, there is a constant absorption of the aqueous particles of the bile going on during the whole time it is stored up in its reservoir. If, then, during the intervals of digestion, the liver secretes merely sufficient bile to meet the requirements of the succeeding meal, by the end of the digestive process the gall-bladder will be entirely emptied of its contents, and ready to receive a fresh supply. Whereas, if the liver secretes more bile during the intervals of digestion than the wants of the system require; after the completion of each succeeding meal the excess of bile will remain behind in the gall-bladder, and, while becoming stored up with that subsequently secreted, of necessity, favour the increase or excite the formation of gall-stones in persons predisposed to them. There being nothing more conducive to the deposition of biliary calculi than a well-filled gall-bladder.

As a warning against the indiscriminate use of podophyllin, I may cite the following case, which has come under my notice as these sheets are passing through the press. A few weeks ago I received a telegram requesting me to visit, as



early as possible, a lady dwelling in the neighbourhood of St. John's Wood. On my arrival I found the lady suffering from a well-marked jaundice, and considerably prostrated in consequence of her having just arrived from Brighton, where she had gone for the benefit of her health, but where, instead of getting better, she got considerably worse. The history of the case was, that the lady had been seized with pain in the back (middle of dorsal region) about three weeks before I saw her. That there had been great tenderness in the region of the gall-bladder—so much so, that she could scarcely tolerate the pressure of her stays; and that she had suffered from occasional attacks of sickness after eating.

On examining the patient I found the liver enlarged, and tender on pressure. The gall-bladder much distended, and easily felt. The skin of a yellow hue. The stools of a pale tint. The urine very dark-coloured, and loaded with lithates. I had, consequently, no difficulty in diagnosing the case as one of gall-stone impacted in the common bile-duct; but on communicating my suspicions to the patient, I was informed that such could not possibly be the case, for during a considerable time past she had been carefully treated with podophyllin. Indeed, I learned to my surprise that she had taken from a quarter to



half a grain of that substance nearly every day during the six previous months!

This incidental piece of information, instead of shaking my opinion, as the patient had apparently expected, only tended to strengthen my suspicions, for the reasons previously given, namely, that the podophyllin must have tended to keep the gall-bladder constantly full of bile. I accordingly prescribed for the case as one of impacted gall-stone, and left instructions that the stools should be carefully examined for its appearance.

On the following day the patient felt better; but the jaundiced tint was deeper, the stools paler, and the urine still high-coloured. The deposit of lithates had, however, slightly diminished. Still, feeling certain that the case was one of impacted gall-stone, I ordered the medicine to be repeated, and the stools to be again carefully examined.\* On my arrival at the patient's house the next day, the maid met me with an expression of satisfaction which could not be misinterpreted, and I had scarcely entered the sick chamber when, with an

\* We are sometimes told to add water to the stools, and that if gall-stones are present they will be found floating on the surface. I have never yet been able to detect a gall-stone in this way. The plan I recommend is, therefore, to mix the stool freely with water, and either decant the supernatant fluid, and then add fresh portions of water till the whole of the soluble matter is removed, or to strain the mixture through a hair-sieve. The gall-stone in either case remains behind, and can be readily detected.



air of triumph, she showed me a gall-stone about the size of a large garden-pea, or small field-bean. It had been passed that morning about 11 o'clock, that is to say about fifteen hours after the second dose of medicine. On analysis the stone was found to consist almost entirely of cholesterine, and I have not the smallest doubt in my own mind that to the constant use of the podophyllin may, in a great measure, be attributed its formation. Unfortunately the stone had been accidentally broken before I saw it, and I was consequently unable to ascertain decidedly whether it was a solitary calculus, or one of many. Had it been one of several, it would of course have possessed facets. One facet would have indicated that the stone was one of two; two facets that three stones existed; three facets, that the gall-bladder had contained at least four calculi; while four or more facets would denote that the stone was one of many; whereas, if it was a solitary calculus, no such markings would be present.

I may merely add, in conclusion, that from the time the stone passed, the stools resumed their normal colour—the first two or three were much darker than natural, in consequence of the sudden escape of the pent-up bile—the urine gradually became pale, and clear, and the skin regained its wonted hue. The latter change was expedited by



the administration of benzoic acid, and in a week from my first visit, a stranger would have been quite unable to detect that the patient had laboured under a recent attack of jaundice.

A few years ago a mixture of sulphuric ether, and turpentine was very extensively used, especially in France, as a solvent for gall-stones. This line of treatment was adopted on account of the well-known solubility of cholesterine in sulphuric ether, and it was thought that the remedy would act upon the cholesterine concretions in the gall-bladder in the same manner as it did out of the body. After a time, faith in the powers of the mixture became shaken, and it at length gradually ceased to be employed.

Within the last year or two, Dr. Bouchut\* has revived the same theory with another form of remedy, namely, chloroform, which he administers internally, with the view of dissolving any inspissated bile or biliary calculi that may be lodging in the gall-bladder. Dr. Bouchut states that he has treated one case of gall-stones in this manner with success. Now, although I have not the slightest desire to throw discredit on the statement of Dr. Bouchut, I must candidly admit that I am very much inclined to doubt the accuracy of his observations. In the first place, it is always

\* "Edin. Med. Journ." 1861, p. 398.



extremely difficult to ascertain the existence of biliary concretions so long as they remain in the gall-bladder, and it is equally difficult to know, after gall-stones have been once passed by a patient, whether or not all have come away. If, then, we administer chloroform to a patient, either before or after a gall-stone has actually passed, we cannot, with anything approaching to certainty, attribute the cessation of his symptoms to the circumstance of the chloroform having dissolved a gall-stone. In fact, on physiological grounds, I very much doubt the efficacy of either sulphuric ether or chloroform as solvents of gall-stones in the living body. Sulphuric ether, and chloroform would no doubt dissolve a concretion of cholesterine in the gall-bladder were they admitted into that viscus in sufficient quantity, and in a pure state. But we have no proof that such is the case. On the contrary, we know, at least in as far as chloroform is concerned, that exactly the opposite is the fact; for no sooner does chloroform become absorbed, and mingled with the constituents of the blood, than it becomes decomposed, the chlorine combining with the blood, and the formic acid being set free.\* And even supposing that sulphuric ether and chloroform existed in the blood in a free state, they could not possibly do so in a sufficiently

\* Jackson, *Comptes Rendus*, February 25th, 1856.



concentrated form to be able to act as solvents of biliary calculi.

My own experiments on animals have shown me how rapidly fatal even small quantities of chloroform are when injected into the circulation, and a similar remark is equally applicable to sulphuric ether. A few drops of these substances can very readily be injected into the circulation with impunity\*; but the quantity must not be increased beyond a certain amount, far less than could possibly dissolve a single grain of cholesterine, otherwise immediate death follows the operation, by inducing a state of body closely resembling rigor mortis, from which the animals never recover. I am, therefore, completely at a loss to understand how these remedies can be of service in dissolving gall-stones in the living body; and as I make it a rule as seldom as possible to prescribe a remedy without a knowledge of its physiological action, I have not yet ventured on an empirical trial of the effects of sulphuric ether or chloroform administered internally in cases of gall-stones. For some remarks on the passage of biliary calculi, see page 123.

\* Vide the Author's paper on a new method of producing diabetes artificially in animals, by the injection of stimulants—alcohol, ether, chloroform, ammonia, &c.—into the portal circulation. *Comptes Rendus de la Société de Biologie de Paris.* 1853.



Taraxacum has been widely used in hepatic disease associated with jaundice, and is believed to be particularly well adapted to cases arising from congestion. As in such cases I generally trust to more potent drugs, my experience with this remedy has been too limited to admit of my offering an opinion of its value.

The majority of cases of jaundice from obstruction, are much less under the power of remedial agents than those arising from suppression, for we have here three distinct conditions to combat: Firstly,—The derangements originating in the absence of bile from the digestive canal. Secondly,—The morbid effects arising from its accumulation in the ducts, and consequent interruption to the hepatic functions. Thirdly,—The general poisonous action on the system, of the re-absorbed bile.

As regards the first of these effects,—namely, the derangements arising from an absence of bile from the digestive canal, it may be said that if these were the only difficulties with which we had to contend in cases of jaundice from obstruction, they could easily be overcome. For, in the first place, the absence of bile is not attended with any immediate danger, a circumstance which has led to the common belief that the presence of bile is not absolutely essential to life. Experiments on dogs



with biliary fistulæ, like those before referred to, as well as cases in the human subject, have proved that life may be sustained, under certain conditions, for a very long period, without bile reaching the intestines. Indeed, the only immediate bad effects which appear to result from its absence, are costive bowels, great flatulence, and extremely offensive stools. The indirect bad results,—namely, loss of flesh, &c., as has been proved by experiments on animals, can be counteracted by giving an additional amount of food; and even the direct results of constipation, flatulence, and fœtor, may be overcome by appropriate remedies.

The secondary morbid effects, namely, those arising from the accumulation of bile in the ducts, are unfortunately not so easily under control. Could we remove the cause of obstruction, these would, of course, immediately cease. This, however, is seldom in our power, except in the case of gall-stones, the expulsion of which we can aid in various ways. In general, we can very successfully aid the passage of a stone through the ducts by administering an anodyne containing a full dose of the tincture of belladonna, which apparently assists in dilating the duct. Placing the patient in a warm bath is also of service; and when the paroxysms of pain are very severe, the occasional inhalation of the vapor from a couple



of drachms of sulphuric ether poured on a handkerchief, made into the form of a cup, is generally attended with great relief. Each of these modes of treatment may be followed either by a brisk emetic, or purgative, in the hope that the efforts of vomiting or purging may hasten the expulsion of the stone, either by the mouth or rectum.

It ought never to be forgotten, that the evil results of a gall-stone do not always cease when it has reached the intestinal canal. Even death itself has resulted from the impaction of a gall-stone in the duodenum. When we have any suspicion that the stone is large, our treatment must therefore be continued until its extrusion by the mouth or rectum has been accomplished.

When the occlusion of the common bile-duct is caused by an organic tumour, no treatment of ours can be expected to remove the obstacle, and sooner or later the patient is carried to an untimely grave. Our efforts of relief in such a case ought therefore to be directed to another channel; and here, in order to give the sufferer at least some chance of recovery, even although it be little better than a forlorn hope, I cannot refrain from recommending, in cases of permanent occlusion of the duct, in which there is great distension of the gall-bladder, the establishment of an artificial biliary fistula. Were this done, the patient would be placed, as



nearly as possible, in the same condition as an animal in which the operation has been performed for physiological purposes, and, we might almost hope, with an equally favourable result, at least, in as far as the biliary functions are concerned. In the first place, we would have removed all the derangements resulting from the interruption to the flow of bile, and consequent upon the distension of the ducts. In the second place, we would have obviated the danger arising from the poisonous effects of the re-absorbed bile, which the experiments previously cited (page 98) show are of no trifling nature; and, lastly, we would only require to combat the evils arising from the absence of the biliary secretion in the digestive process, which, as was before said, can to a certain extent be overcome by giving an additional quantity of food, and paying attention to the bowels. In these remarks I have omitted taking into consideration the effects that might arise from the tumour, or other obstructing cause to the biliary secretion, for these would in no way be directly influenced by the establishment of the biliary fistula.

The artificial establishment of a biliary fistula in the human subject, is not such an Utopian idea as might at first be imagined. Distended gall-bladders having been several times tapped with



success, both in this and other countries, and the permanent establishment of a fistula, if done in the manner I shall immediately point out, would, in my opinion, be a much less hazardous operation than simple tapping. Biliary fistula in dogs are generally made in a single operation, by cutting through the abdominal parietes, seizing the gall-bladder, stitching it to the lips of the wound, and inserting a cannula. Here there is always some danger of the wound not healing by the first intention, and of the passage of bile into the abdominal cavity. In the case of the human subject, I should, therefore, recommend the inducing of the adhesion of the gall-bladder to the abdominal parietes by means of an escharotic, before making the opening; in which case, I can scarcely imagine that the operation would prove one either of difficulty or danger. But even supposing that it were not entirely free from either, it would still surely be preferable to give the patient at least a chance of prolonging his life, rather than to permit a fatal affection to run its uninterrupted course, which we know can, at best, be calculated by months only.

In those cases of jaundice from obstruction, where it might be considered inadvisable to adopt the plan here suggested, we ought in our treatment carefully to avoid the common error of ad-



ministering mercury, or other substances supposed to have the power of augmenting the biliary secretion. We must equally avoid the administration of foods likely to produce a similar effect, for the sufferings of the patient are not so much due to a deficient secretion, as to a want of biliary excretion. Our whole energies should be directed to sustaining the strength of the patient, and mitigating, if possible, the physical effects of the accumulation of the bile in the gall-bladder and biliary ducts, as well as the poisonous action of the re-absorbed secretion. This, I believe, we can best do by administering light and readily digested food, keeping the bowels open by gentle purgatives, and favouring the elimination of the biliary constituents from the blood by mild diuretics. Our object may be still further advanced by artificially supplying the place of the absent bile in the digestive process. *Not, however, in the way usually adopted, of giving inspissated bile along with the food;* a method of treatment which originated ere modern physiology rent the veil of therapeutical empiricism. In the first place, the bile prepared according to the method indicated in the pharmacopœias, has its most essential properties destroyed during the process of preparation. And in the second place, we have hitherto been instructed to administer it



at the very time which modern research has proved to be the most unsuitable that could possibly be devised. In administering bile immediately after food, as is usually done, we most effectually produce the contrary result to what is intended. When bile mingles with gastric juice, it destroys the digestive power of the latter, so that by giving the bile immediately or soon after a meal, we really diminish instead of increase the digestive functions. My experiments, both chemical, and physiological, have led me to propose not only a new method of preparing bile for medicinal purposes, but also to suggest an entirely new mode of administering it.

Firstly,—As regards the method of preparation. Nothing can be more simple, and at the same time more effectual. Fresh bile, taken directly from the gall-bladder of the newly killed pig, is filtered, through very porous filter-paper, to free it from mucus; it is then as rapidly as possible evaporated to dryness at a temperature not exceeding 160° Fahr. The bile, as soon as dried, is ready for use. Simple as this operation appears in theory, there are two practical difficulties connected with it—1st, Bile filters very slowly, and consequently little must be put into the filter at a time. 2nd, Bile is rather hygroscopic, and consequently, in order to get it dried quickly, it is necessary



to spread it over a large surface. If the bile has been well prepared, that is to say, thoroughly freed by filtration from its ferment mucus, and well dried, it will keep in stoppered bottles for many months without losing any of its active properties.

Having stated that bile as at present employed more frequently does harm than good, by retarding instead of hastening the digestive process, I have now to point out the manner in which it may be given with advantage.

If bile be administered, as I propose, at the *end* of stomachal digestion, it will, as in the healthy organism, act on the chyme at the proper moment, and thereby render it fit for absorption. In order still further to ensure the action of the bile being delayed until the food is in a condition favourable to its action, that is to say, until it is ready to pass from the stomach into the duodenum, I have had the bile, as above prepared, put into capsules,\* which are not readily acted on by the gastric juice. While in the stomach, the capsules, however, swell up from the size of a pea to that of a small gooseberry, and at the same time become so soft that they will readily burst in passing the pylorus into the duodenum, and thereby allow

\* The capsules were made by Savory and Moore, and I have every reason to be satisfied with the manner in which they accomplished the object in view.



the bile to escape, and come in contact with the food at the precise moment its action becomes requisite in the digestive process.\* The capsules not only preserve the active properties of the bile for an almost indefinite period, but they have the advantage of most effectually preventing the patient tasting the remedy.

Each capsule contains five grains of the prepared bile; and five grains is equal to one hundred grains of liquid bile fresh from the gall-bladder. Two capsules therefore represent two hundred grains of pure bile, a quantity (though less, perhaps, than the healthy organism consumes during each digestion) which in most cases would be sufficient for the wants of the system. If, however, a larger amount be considered necessary, there is no reason why three or more capsules should not be given. By the administration of prepared bile in the manner here described, the physician is enabled to imitate nature, and sup-

\* Prepared bile, made up into an ordinary pill, dissolves in gastric juice in a quarter of an hour. When the pill is silvered it is dissolved in half an hour, and when gilded, in forty minutes. Whereas, in the same specimen of gastric juice, the capsules prepared for me by Savory and Moore, although swollen to more than three times their original size, were nevertheless intact at the end of an hour and a half. They readily broke on being gently squeezed between the finger and thumb, it is not therefore probable that they would pass the pylorus in this condition without giving way, and allowing their contents to escape.



ply an important element to the system; which, although incapable of curing the disease, can nevertheless ward off for a time the fatal termination.\*

\* It is not alone in cases of jaundice that the prepared bile may be of service, but also in the various forms of duodenal dyspepsia, so common among the literary classes, consequent upon either a deficient quantity, or an abnormal quality of bile.



TABULAR VIEW OF THE PATHOLOGY OF JAUNDICE,  
ACCORDING TO THE AUTHOR'S VIEWS.

Jaundice.	From Suppression.	Enervation.	{	Fright.
				Anxiety.
				Over-mental exertion.
		{	{	Concussion of Brain.
		Congestion of Liver.	{	Hepatitis.
				Direct Violence.
	{	Active.	{	Dyspepsia.
				Ague.
	{	Passive.	{	Typhus.
				Typhoid.
	{	Absence of Secreting Substance.	{	Scarlatina.
				Pyæmia.
	{	Congenital Deficiency of Ducts.	{	Yellow Fever.
				Poison.
	{	Accidental Obstruction in course of Duct.	{	Heart-Disease.
				Pneumonia.
	{	Closure of Outlet.	{	Pleurisy.
				Imperfect Circulation in the New-born.
	{	From Obstruction.	{	Cancer.
				Cirrhosis.
	{	Congenital Deficiency of Ducts.	{	Fatty Degeneration.
				Amyloid do.
	{	Accidental Obstruction in course of Duct.	{	Atrophy { Acute.
				Chronic.
	{	Closure of Outlet.	{	Small Ducts (?)
				Common Duct.
	{	From Obstruction.	{	Gall-stones.
				Hydatids.
	{	Closure of Outlet.	{	Foreign Bodies from Intestines.
	{	From Obstruction.	{	Pressure of Pregnant Uterus.
				Impacted Fæces in Transverse Colon.
	{	Closure of Outlet.	{	Organic Disease of Pancreas, or of neighbouring Organs.
				Abscess in Head of Pancreas.
	{	From Obstruction.	{	Ulcer of Duodenum.



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