THE GOULSTONIAN LECTURES ON THE CHEMISTRY AND PATHOLOGY OF GOUT.

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By ARTHUR P. LUFF, M.D., B.Sc., F.R.C.P.,

Physician in charge of Out-patients in St. Mary's Hospital; and Lecturer on Forensic Medicine in St. Mary's Hospital Medical School.

[ABSTRACT.]

LECTURE I.

WHEN I accepted the duty of delivering the Goulstonian Lectures for this year I was deeply sensible of the honour conferred upon me, and of the serious responsibility that I incurred. As the youngest Fellow of this College I should, perhaps, not have ventured to discourse to you on the subject of gout—a subject which has been so enriched and so ably dealt with in the past by many distinguished Fellows of this College—were it not that I thought the occasion was a convenient one briefly to review the various opinions held as to the causation and nature of gout, and, at the same time, to place before you the results of some experimental work that I have been conducting on the chemistry and pathology of this disease. As I propose to continue and extend this line of work, I can only in these lectures lay before you the results that I have so far obtained, and the conclusions I have arrived at from those results. I must, therefore, request your indulgence for the somewhat fragmentary nature of the experimental work.

Gout is the manifestation of a number of morbid tendencies, some of which may be inherited and some acquired, and which result in the different diseases associated with the arthritic diathesis. If the joints are affected articular or regular gout results; if other organs or tissues are affected then irregular gout is produced.

Gout is associated with the presence of an excess of uric acid in the blood, and the questions I propose to discuss in these lectures mainly resolve themselves into the mode or modes by which the uric acid is produced and introduced into the blood, the source or sources of its production, the relationship that it bears to the gouty paroxysm and to the other manifestations of gout, and the factors or conditions which influence its formation and its injurious action.

Uric acid was discovered in the urine by Scheele in 1775, and in 1787 Wollaston demonstrated its presence in gouty concretions. It was not, however, till 1847 that Sir Alfred Garrod first found uric acid in the blood of gouty patients in the form of a sodium salt.

The various views held as to the primary cause of gout may be classified into the three following groups:

1. Excess of uric acid regarded as the primary cause.
2. Morbid changes in the structure of tissues regarded as the primary cause.
3. Nervous disturbance regarded as the primary cause.

1. EXCESS OF URIC ACID REGARDED AS THE PRIMARY CAUSE OF GOUT.

(1) *The Uric Acid Compound regarded as Acting Passively and Physically while in the Crystalline State.*—Sir Alfred Garrod and Sir William Roberts are the two principal exponents of the view. The former regards the inflammation attending each paroxysm of gout as the mechanical effect of the deposition of sodium biurate in an articular cartilage predisposed to its reception by being the seat of former injury or disease. The deposition is determined by the blood for some reason or other becoming incapable of holding the compound in solution. Sir William Roberts also regards uric acid in solution as innocuous, harmful effects accruing only from its crystallisation in the blood and tissues. He attributes irregular gout to the precipitation of sodium biurate crystals in the structures of the organs implicated, and considers that scattered needles of the salt may form the foci of gouty thromboses. Such crystals have been found by Cornil and others in the neurilemma of peripheral nerves, in the cerebral meninges, and elsewhere.

(2) *The Uric Acid Compound Regarded as Acting as a Poison or Irritant while in the Dissolved State.*—Many writers and

observers have supported the view that, apart from the local trouble in the joints caused by the deposited sodium biurate acting as an irritant, the soluble uric acid compound which is circulating in the fluids of the body acts as a poison, the toxic effects of which are responsible for a number of the symptoms associated with the gouty state.

Pfeiffer holds that a compound of uric acid is deposited, without ill effect, in both healthy and diseased parts of the body, and that an acute attack of gout is caused by some of this being redissolved by increased alkalinity of the blood to form a concentrated solution with toxic properties. But we know that uric acid is deposited as the sodium biurate, and it will be shown later on that the solubility of this is not heightened by increased alkalinity of the solvent.

Sir W. Roberts advances against the toxicity of uric acid in solution, first, the absence of experimental proof, and, secondly, the fact that on the eve of an attack of acute gout the fluids of a patient's body are saturated with sodium biurate, and yet no toxic symptoms precede the arthritic manifestations. Furthermore, in leucocythæmia and other severe anæmias the blood is frequently highly charged with uric acid, but toxic symptoms are entirely absent.

Kolisch considers that gout is produced by the accumulation of alloxur bases and similar precursors of uric acid in the blood owing to defective action of the kidneys, which normally convert them into uric acid, as which they are excreted. He is supported by Weintraub, but opposed by Schmoll, who fails to find increased excretion of alloxuric bodies in chronic gout.

2. MORBID CHANGES IN THE STRUCTURE OF TISSUES REGARDED AS THE PRIMARY CAUSE OF GOUT.

(1) *Necrotic Changes in the Affected Tissues due to the Presence of Dissolved Urates regarded as the Primary Cause of Gout.*—Ebstein,¹ who is the main exponent of this view, holds that a necrotic process is produced in the cartilages or other implicated tissues by uric acid in one form of combination, as the result of which uric acid in another form of combination is deposited in the necrosed areas, uratic crystals forming only in necrosed and never in healthy tissues. He holds that the neutral sodium urate in a dissolved state acts as an irritant, causing venous stasis, and eventually necrosis in the implicated tissues. The process of necrosis generates a free acid, which converts the neutral urate present in the fluids of the body into the acid urate, which is accordingly deposited in the necrosed tissues.

Ebstein bases his theory on two sets of experiments, the first of which consisted in the examination of the organs and tissues of birds which he had endeavoured to render gouty by preventing the elimination of their urinary secretions; the second in observations of the irritant effect of sodium urate solution upon the cornea. The first research was carried out in two ways (a) by ligaturing both ureters of cocks, (b) by administering to them repeated small subcutaneous injections of neutral potassium chromate, which he considers to inhibit the passage of uric acid through the kidneys by its action on the renal parenchyma, both methods resulting in the formation of uratic deposits in the articulations, tendon sheaths, liver and muscles; these deposits were much larger in the latter case, in which the animals could be kept alive for a longer period. He concluded that a necrotic process had supervened upon the action of some necrotic agent (presumably uric acid) and had led to the deposition of the urate.

I do not think that the morbid processes occurring under these conditions in fowls can be considered as in any sense comparable with those occurring in connection with gout in man. Ebstein found uratic deposits in the liver and muscular tissues of the birds experimented on—localities where they are not found, at all events to any appreciable extent, in human gout. From this one may fairly conclude that the two processes cannot be considered as comparable. Moreover, since the fowl produces and eliminates by the kidneys so large a quantity of urates, the more or less sudden stoppage of kidney excretion must necessarily result in the damming back of it and the rapid accumulation of it in the blood and tissues, where, as Sir William Roberts² suggests, it would probably first collect in a state of solution as the quadriurate, which would then be precipitated in the tissues as the gelatinous biurate, and this in its turn would be changed into the crystalline biurate.

The second series of experiments, which Ebstein regards as proving that sodium urate is the cause of tissue necrosis, consisted in the injection of a saturated solution, prepared at 100° F., of uric acid in 5 per cent. sodium phosphate into the peritoneal cavity, anterior chamber, cornea, and other organs of a rabbit; further, in the introduction of uric acid in powder into the conjunctival sac. By comparing the result of this upon the cornea with that of injecting a simple solution of sodium phosphate or water containing calcined magnesia in suspension,

he arrived at the conclusion that uric acid and its salts produced definite necrotic changes.

The objection to this method of experimentation is that, in the first place, the solution of uric acid in sodium phosphate does not contain the neutral sodium urate, which is the body on which Ebstein relies for the production of the initial irritant effects leading on to the necrotising process. The solution would contain the sodium quadriurate, or the biurate, or a mixture of the two. Moreover, as Sir William Roberts has pointed out, such a saturated solution would soon begin to deposit its urate in the form of the gelatinous biurate, which, infiltrating the affected area of the corneal tissue, would act as a mechanical irritant. It is clear, therefore, that all the corneal changes observed by Ebstein can be accounted for by the assumption that they are caused by a mechanical irritant.

Neubauer's experiments, in which he administered enormous quantities of uric acid to rabbits without causing any apparent inconvenience, also oppose this view. Moreover, it may well be asked why, if urates are to be regarded as irritants, the kidneys, which normally excrete them constantly, ever escape damage. Furthermore, not only is there no proof that the neutral sodium urate which Ebstein regards as starting the gouty changes ever exists in the human body, but there is strong evidence that it never can so exist, as it is an extremely caustic and unstable body which is decomposed in the presence of carbonates such as those in the blood. And Pfeiffer has shown that the injection of strong solutions of the biurate cannot cause necrosis, a result which must apply still more to the weak solutions found in the blood. Ebstein's further assumption that the necrotic process generates an acid converting the neutral into the acid urate shows an imperfect acquaintance with the chemistry of the subject; for Sir William Roberts has shown that uric acid is primarily taken up by the blood and lymph not as a neutral urate but as a quadriurate, and that the formation and deposition of the crystalline biurate are not favoured by the intervention of an acid. Ebstein's assertion that he is able to demonstrate necrotic changes in areas from which he has dissolved out crystalline urates in not in accord with the results of other competent observers, and I myself have been unable to find in such cases any changes beyond what might be produced by mechanical pressure followed by some inflammation and degeneration.

If, too, the sodium biurate is only formed and deposited in necrosed areas, how is it that crystals of sodium biurate are occasionally found free in the synovial fluid of a gouty joint? As Sir William Roberts' remarks, "it will scarcely be contended that necrotising and necrotic processes can take place in synovia."

Sir Dyce Duckworth,⁴ in a modified sense, believes that a soluble urate may act as an irritant. Although he considers that gout is primarily due to a disorder of the nervous system, he entertains the additional view that the urate in solution may set up degeneration and necrotic changes in tissues.

(2) *Inflammatory or Degenerative Changes in the Affected Tissues regarded as the Primary Cause of Gout, such Initial Changes not being caused by Urates.*—Dr. Ord in 1872 considered that gout was due to a special form of degeneration in some of the fibroid tissues, resulting in an excessive formation of sodium urate, which is then discharged into the blood, and is subsequently deposited in those parts least freely supplied with vascular and lymphatic structures. Dr. Ord, whose views in this particular have been supported by Dr. Norman Moore and Mr. Bowlby, also considers that uratic deposits only occur in tissues which have previously begun to degenerate.

Dr. Berkart holds that the uratic deposits are most frequently connected with a form of panarthritis chiefly affecting the smaller joints of the extremities. This probably originates in some kind of atrophy of the bone, followed by degeneration of the cartilages and fibrous tissues of the joints, leading to necrosis of the tissues close to or within the joint. The necrosis is the cause of the local symptoms, and the whole process results from a profound disturbance of nutrition.

Dr. Berkart attributes the presence of the urates in the blood in part to leucocytosis, and in part to the formation of uric acid from the disintegration of the tissues; so that he regards the uratic deposits as an epiphenomenon, and not as the cause of the gouty paroxysm.

3. NERVOUS DISTURBANCE REGARDED AS THE PRIMARY CAUSE OF GOUT.

Cullen, the great opponent of the humoral theory in the

latter half of the last century, considered that gout mainly depended on an affection of the nervous centres. Sir Dyce Duckworth,⁵ while accepting the view as previously mentioned, that uric acid has some connection with gout, considers that gout is primarily dependent on a functional disorder of a definite tract of the nervous system, and that the part specially involved is possibly situated in the medulla oblongata, where, it may be, there is a trophic centre for the joints. One reason that Sir Dyce Duckworth⁶ gives for considering this possible is the relationship of gout to diabetes, the consideration of which has led him to the belief that the portions of the nervous system involved in the two diseases cannot be far apart from one another. In consequence of this disorder of the neurotrophic system defects of nutrition arise, which not only cause undue formation of uric acid, but also inhibit the normal destruction of that body in the tissues; at the same time the renal excretory power for uric acid appears to be temporarily inhibited as part of the process of the gouty paroxysm. He draws the following distinction between inherited and acquired gout: In primary, or inherited, gout the toxæmia is dependent on the inherited gouty neurosis. In secondary, or acquired, gout the toxæmia arises from the digestive and excretory organs becoming overloaded, and then if with this toxæmia there is depression and exhaustion of the nervous system, the gouty neurosis may be established by the morbid blood condition affecting the nutrition of the nervous system.

Dr. Edward Liveing⁷ considers that there is much to be said in support of the view that gout is a manifestation of a disorder which has its primary seat in the nervous system.

Dr. P. W. Latham⁸ regards some change in the nervous system as the most important factor in the etiology of gout. He thinks that such change is localised in the medulla oblongata, or the spinal cord, or in both, and that this nervous disorder may be either hereditary or acquired. He argues that if a portion of the medulla oblongata involving some of the roots of the vagus be the part affected the metabolism of the liver may be interfered with, and so lead to the formation of uric acid. He also considers that if from any cause uric acid is circulating in the blood it would act as a poison upon any weak spot in the nervous system, and that it is intelligible that it might act upon portions of the spinal cord which control the nutrition of the joints, and so cause nutritive changes or inflammation in the joints connected with that portion of the cord. In consequence of the inflammation or nutritive changes in the joints sodium biurate becomes deposited in them or in the tissues around the affected joints. Dr. Latham explains the phenomena of a gouty paroxysm by direct stimulation of sensory nerves by uric acid. He considers that the gout associated with chronic lead poisoning may be explained by the lead acting in such cases more particularly on such portions of the spinal cord which are concerned in gout.

Dr. Ralfe held the view that the accumulation of uric acid in the blood in gout was due to non-conversion into urea of the uric acid normally formed in the tissues, and he considered that the conditions which prevent the normal destruction of uric acid in the tissues depend probably on disturbance of innervation. From a careful consideration of these various views as to the primary cause of gout I am of opinion that the greatest mass of evidence is in favour of the view that a compound of uric acid is the *materies morbi*.

All observers are agreed that an abnormal quantity of uric acid is found in the blood in gout. This over-charging of the blood with uric acid must be due to one or more of the following causes:

1. Normal production and deficient excretion of uric acid.
2. Over-production and normal excretion of uric acid.
3. Diminished destruction of uric acid by imperfect oxidation, or by some other means.

This last theory may be dismissed at once. There is no proof that the process of oxidation destroys uric acid; on the contrary, there is proof that uric acid is produced by a process of oxidation. Moreover, not only is there no proof that uric acid is produced during health in the organs and tissues of the body generally, and that it subsequently undergoes more or less destruction, but there are good reasons for believing that uric acid is, in health, only formed in the kidneys, and never appears in the general circulation except under pathological conditions.

With regard to the second theory of over-production and normal excretion of uric acid, there is abundant experimental proof to show that an increased production of uric acid, as in leucocythæmia and severe anemia, does not lead to gout so long as the kidneys remain in a normal condition. In addition gout is essentially a disease of middle age, and is only very exceptionally met with in childhood and in youth,

although the formation of uric acid is greatest in early life, and apparently diminishes with the advance of age.

View that Deficient Excretion of Uric Acid is Connected with Gout.—That there is a deficient excretion of uric acid in gout is, I think, justified by the following facts. Judging as far as is possible by averages, recent accurate estimations of the excretion of uric acid show that in gouty subjects there is a decrease in its daily excretion, as compared with healthy individuals.

Pfeiffer⁹ compares the quantities of uric acid contained in the urine of gouty patients of various ages, and in whom the complaint had not yet become chronic, with the quantities contained in the urines of subjects at the same age. For purposes of comparison the quantities of uric acid found by him were calculated in grammes per 100 kilogrammes of the body weight. His results are given in the following table:

Age.	Gouty Subject.	Healthy Subject.
	Gramme.	Gramme.
30 to 40	0.885	0.965
40 to 50	0.818	0.882
50 to 60	0.701	—
60 to 70	0.661	0.752

This table indicates that the amounts of uric acid excreted by gouty subjects were always rather lower than the quantities excreted by healthy persons of the same age.

In the following table are the results of the daily determinations that I made for eight successive days respectively of the total uric acid excretion in the urine of three persons, namely: (a) a male patient suffering from an attack of subacute gout supervening on chronic gout; (b) a male patient suffering from chronic gout and lead poisoning, with recent pain in the right metatarso-phalangeal joint, and in both ankle-joints; (c) a healthy man. The quantities of uric acid in the three cases are given in grammes, and are calculated per 100 kilogrammes of the body weight. All the individuals were between 40 and 50 years of age:

Subacute Gout.	Chronic Gout.	Healthy Subject.
Gramme.	Gramme.	Gramme.
0.260	0.578	1.105
0.263	0.617	1.027
0.315	0.665	1.020
0.350	0.715	1.376
0.442	0.443	1.175
0.556	0.372	1.030
0.506	0.593	1.252
0.494	0.594	1.203
Average 0.398	Average 0.572	Average 1.148

These results, I think, justify the view that deficient excretion of uric acid occurs in connection with gout. I shall have occasion in a subsequent lecture to discuss in detail the probable rôle taken by the kidneys in the production of uric acid and in the development of gout.

Estimation of Uric Acid in Urine.—After repeated trials of the various methods which have been recommended for this purpose, I have come to the conclusion that the one devised by Mr. Gowland Hopkins¹⁰ is by far the most reliable, and I have accordingly adopted it in my experiments. It consists in saturating the urine with powdered ammonium chloride, allowing it to stand for two hours, with occasional stirring, and then filtering. The precipitated ammonium urate is washed three or four times with saturated ammonium chloride solution, washed off the filter into a small beaker with a jet of hot distilled water and heated just to boiling with excess of hydrochloric acid. The beaker and contents are allowed to stand in the cold for two hours, when the uric acid separates out completely and is collected on a filter and washed with cold distilled water. [The filtrate should be measured before washing and 1 mg. added to the final result for each 15 c.c. of filtrate.] The uric acid is washed off the filter with hot water, warmed with sodium carbonate till dissolved, then transferred to a flask and mixed with 20 c.c.m. of pure sulphuric acid. The mixture is titrated warm with a twentieth normal solution of potassium permanganate till a permanent pink colour is obtained; 1 c.c.m. of the permanganate = 0.00375 g. uric acid.

Quantitative Determination of Uric Acid in the Blood.—I have tested the methods devised by Salkowski and Leube, von Jaksch, and Klemperer by adding a known percentage of uric acid to bullock's blood which I had proved free from that substance, and then endeavoring to estimate it in the mixture. Very erroneous and discordant results being obtained, I devised the following plan, which I have used exclusively in my experiments: The fresh blood is allowed to flow direct into its own volume of rectified spirit (containing 2 per cent. formalin to prevent decomposition), with which it is agitated. The mixture is evaporated to dryness over a

water-bath and the resulting solid finely powdered; 100 g. of the powder (=500 of the liquid blood) are mixed with a litre of boiling water, the whole being kept boiling for half an hour and then filtered, first through glass wool and then through filter paper. The filtrate is evaporated to 50 c.c.m., again filtered, and finally subjected to the Gowland Hopkins process for the estimation of uric acid. By this means 80 to 87 per cent. of the uric acid can be extracted, but no more, and I have found no solvent of greater power than the distilled water.

Admitting that an excess of uric acid in the blood, and that its deposition therefrom in cartilages and other tissues is the direct exciting cause of a gouty paroxysm, the two questions that naturally arise in the mind are: 1. Where is the uric acid formed? 2. How is the uric acid formed? I believe that uric acid is formed in connection with some diseases, notably blood diseases accompanied by leucocytosis, in a different manner to that in which it is produced in health, and also in different organs. I also hold the opinion that the source of the uric acid contained in the blood in gout is the same as that from which the uric acid eliminated in the urine in health is derived. I propose, therefore, first to consider the various views as to the seat or seats of formation of uric acid in health and in gout.

SEAT OR SEATS OF FORMATION OF URIC ACID IN HEALTH AND IN GOUT.

View that the Kidneys Form as well as Excrete Uric Acid.—This theory is maintained by Sir Alfred Garrod,¹¹ who concludes that uric acid in the blood, if not absorbed from the stomach, must arise from that formed in and by the kidneys, the blood changing the salt from the ammonium to the sodium urate. Kolisch¹² also regards the kidneys as the most important of the uric-acid-forming organs. Dr. Latham considers that the kidney is the seat of the final formation of uric acid by the conjugation of substances manufactured in the blood. Zalesky compared the effects of extirpating the kidneys and of ligaturing the ureters in serpents, which excrete almost pure uric acid; the animals lived about the same time in either case, but in the latter only were uratic deposits found in the tissues. This he takes to confirm the above theory, which is supported also by the observation of Garrod and others that the administration of uric acid or its injection into the blood caused an increase of urea in the urine, but not of uric acid.

View that the Liver and Spleen Produce Uric Acid.—The view that the liver is the main manufactory of uric acid probably depends on the fact that the excretion of this substance is greatest during digestion; this fact is, however, compatible with the idea that the liver forms only the precursors of the acid which are combined in the kidney. Schroeder states that uric acid is normally found in the blood of birds, and that it continues to be formed and, indeed, accumulates in the liver and blood after the removal of the kidneys. This is directly opposed to Zalesky's experiments; further, if uric acid is formed in the liver and conveyed to the kidneys, it must be present in the blood, and I shall shortly show that the blood of birds is entirely free from uric acid. Minkowski¹³ succeeded in keeping geese alive from six to twenty hours after extirpation of the liver; after the operation their urinary excrement contained only 2 or 3 per cent. of uric acid, instead of the normal 60 or 70 per cent. These results are, however, equally compatible with the view that the liver is the seat of production of the antecedents of uric acid.

Dr. Murchison regarded the liver as the seat of production of uric acid, and the presence of the latter in the blood or tissues as the result of functional derangement of the liver, as the result of which the metabolism of some of the albumen is arrested at the stage of uric acid formation, instead of going on to the complete stage of urea formation. Charcot regarded the liver as the principal seat of production of uric acid. He considered that a functional derangement of the liver caused the production of excessive quantities of uric acid, and its consequent accumulation in the blood. Meissner regards the liver of fowls in the normal condition as the principal source of uric acid, but considers that the spleen and the nervous tissues share in the formation. Ranke was of opinion that his experiments led to the conclusion that the spleen was the principal organ concerned in the production of uric acid. It has, however, never been possible to show that the spleen takes any active part in developing the gout.

Views that Uric Acid is produced in various Tissues.—Ebstein,

who attributes in cases of gout the main production of uric acid to the muscles and bone marrows of the affected extremities, admits however that the kidneys may take a part, not only in the secretion, but also in the manufacture of uric acid. Robin was the first to suggest that uric acid was normally formed in all the tissues, and that the condition in gout was only an exaggeration of the physiological one. Chrzonszczewski, Cantani, and Senator also considered that uric acid is formed in cartilage and fibrous tissue, but most observers agree that it is only deposited, and does not originate in tissues of the connective group. Dr. Haig asserts that in addition to the formation of uric acid in the animal body, the amount present depends greatly on that taken in. He does not, however, produce any proof of the storage of uric acid in the system apart from gout, and it must further be remembered that in diseases such as leucocythæmia, in which large quantities of uric acid are formed, they are not stored but eliminated.

Does Uric Acid occur Normally in the Blood of Man and other Animals?—The solution of this question is of great importance in relation to the problem as to whether uric acid is formed in or carried to the kidneys. I am able to confirm the conclusions of Garrod, von Jaksch, and Klemperer that uric acid is absent from the blood of healthy persons. Of other mammals I have examined the blood of the ox and sheep, and have found no trace of uric acid in them, a result which is again in accordance with those of Sir Alfred Garrod. In the blood of the turkey, goose, duck, and fowl I found, like him, no uric acid, but plenty of urea. Sir John Davy also failed to find uric acid in the blood of snakes.

This mass of experimental evidence, which shows that uric acid is never present in the blood of human beings in health, and also that it is never present in the blood of birds and serpents, although their urinary excretion is almost entirely composed of a compound of uric acid, conclusively supports the view advanced by Sir Alfred Garrod, and held by Dr. Latham, and in a modified sense by Kolisch, that uric acid is normally produced in the kidneys. How is it possible in all these cases that uric acid could be absent from the blood if the view be correct that uric acid is formed in the system generally, and is conveyed in the blood to the kidneys, which play, as it were, merely the part of a filter in the removal of uric acid from the blood? I consider that the evidence brought forward renders such a view impossible.

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LECTURES

ON

DISEASES OF THE GALL BLADDER
AND BILE DUCTS.

Delivered at the Royal College of Surgeons of England.

By A. W. MAYO ROBSON, F.R.C.S.,

Hunterian Professor of Surgery and Pathology, Royal College of Surgeons of England.

LECTURE III.

GALL STONES OR CHOLELITHIASIS.

THE importance of this subject may be gathered from the facts that *post-mortem* records on persons of all ages and both sexes prove gall stones to be present in from 5 to 10 per cent. of all Europeans, in Strassburg the record being 12 per cent. (Schroeder), in Kiel 5 per cent., and in Manchester 4.4 per cent. (Brockbank).

Surgical Treatment.—After medical treatment has been fairly and fully tried, and failed, I think all are now agreed that surgical measures should be resorted to. While cholecystotomy is generally recognised as the operation to be aimed at in the treatment of affections of the gall bladder or bile ducts, especially in cholelithiasis, it is often impossible

to say what operation will have to be done until the abdomen is opened.

The indications for operating would seem to me to be as follows:

1. In frequently recurring biliary colic without jaundice, with or without enlargement of the gall bladder.
2. In enlargement of the gall bladder without jaundice, even if unaccompanied by great pain.
3. In persistent jaundice ushered in by pain, and where recurring pains, with or without ague-like paroxysms, render it probable that the cause is gall stones in the common duct.
4. In empyema of the gall bladder.
5. In peritonitis, starting in the right hypochondrium.
6. In abscess around the gall bladder or bile ducts, whether in the liver, or under, or over it.
7. In some cases where, although gall stones may have passed, adhesions remain and prove a source of pain and illness.
8. In fistula, mucus, muco-purulent, or biliary.
9. In certain cases of chronic jaundice, with distended gall bladder dependent on some obstruction in the common duct, although the suspicion of malignancy be entertained. In such cases the increased risk must be borne in mind, as malignant disease may be the cause of the obstruction, and operation in such cases is attended with greater danger than ordinary.
10. In phlegmonous cholecystitis and in gangrene, if the case be seen and recognised at a sufficiently early stage of the disease.
11. In gunshot injury, or in stab wounds over the region of the gall bladder.
12. In suspected rupture of the gall bladder without external wound.
13. In some cases of chronic catarrh of the gall bladder or bile ducts.
14. In suppurative cholangitis.

Of the operative measures undertaken for diagnosis, sounding and aspiration of the gall bladder must be referred to. The former is both uncertain and dangerous, and may more safely be replaced by a small exploratory incision, which can be extended for treatment if required. Aspiration of a distended gall bladder through the unopened abdomen, though apparently a simple procedure, is not unattended with danger, death having followed in more than one instance. Murphy says it is fatal in 25 per cent. It is only in very exceptional cases that it can do any good. Here, again, I infinitely prefer to make a small exploratory incision, then to empty the gall bladder by the aspirator, and afterwards to explore the bile passages with the fingers. If, however, aspiration without exploration be decided on, a small needle should be used and the cyst emptied as far as possible, in order that intracystic tension may not lead to extravasation through the needle puncture. With regard to technique, it may be well for us first to consider a simple abdominal section in the gall-bladder region.

Position of Patient.—It has been proposed to suspend the upper part of the trunk when the patient is on the operating table by straps placed under the armpits in order to allow the intestines to fall away from the liver, and thus to afford a better view of the parts to be operated on, just as the Trendelenburg position does in the case of the pelvic organs; but this is inconvenient, and, as a rule, impracticable. I think it will be found that a narrow firm sand bag covered with flannel, placed at the liver level on the operating table under the back, which is thus arched over it, will do all that we require, as it brings the common duct from 2 to 3 inches nearer the surface, opens out the costal angle, and tends to make the intestines slip down from the liver.

Incision.—A vertical incision in the right semilunar line is the one I prefer. If more room be required it can be obtained either by extending the vertical incision or adding a transverse one, either internal or external to the vertical line. It is advisable to avoid as much as possible dividing muscular fibres, as they retract and can only with difficulty be approximated in suturing the wound. The transversalis fascia and peritoneum are best divided together, without separating them, as together they form a strong membrane, whereas singly they are too weak to hold stitches if there be tension. Kocher employs an oblique incision parallel to the right costal margin, which of necessity divides muscle, but which exposes the parts freely, as the wound at once gapes widely. Although for cholecystotomy the transverse incision is quite unnecessary and to my mind usually inadvisable, where it is necessary to expose or manipulate the common duct it presents the advantages of better exposure and more efficient drainage.

Arrest of Hæmorrhage.—As a rule pressure forceps and an occasional ligature effect all that is desirable or necessary, but in cases of long-standing jaundice, especially if accom-