consisting of one part of boric acid, one part of zinc oxide, and two parts of fine starch powder, is helpful to keep the skin dry where the pads press.

Tact, persuasion, and sometimes a little threatening, all have to be used in dealing with patients, particularly with those who, having been careless, have allowed their hernias to get out of control. It is wonderful how a comfortable and efficient truss conscientiously worn will diminish the size of the protrusion of the hernia; so much so that sometimes a patient will consider himself cured and unwisely discontinue with the truss, and then find that the hernia recurs.

Not very infrequently the application of a truss to an easily reducible but large hernia will render a subsequent operation more simple and more sure of satisfactory results.

Durability.

All the materials from which a truss is made must be good, and one made from cheap materials will wear out in a short time. Hence a good truss made by hand from the best materials cannot be a cheap article, but one for which a good price must be paid.

Well-tempered steel, made as far as possible rustless, reliable leather covering, and neat sewing all tend for long life of the appliance and satisfaction to the wearer. It is distressing to see the shoddy specimens sometimes sold even by respectable firms, and all practitioners should know a good truss from a bad one.

Economy in Cost.

From what has been said the real economy in cost is to have, in the first instance, a well-made, well-fitting, and durable truss. Then to secure a second one made of the same type as soon as it is proved that the original is satisfactory, and to counsel the patient to wear them alternately week by week. In this way each will last longer, and, should one happen to go wrong, there is the other already comfortable and ready to wear whilst repair or renewal is being carried out.

In the treatment of herniae by trusses close co-operation is required among all the three parties concerned—the patient, the practitioner, and the manufacturer. Personally I am certain that the patient should not go to the manufacturer, but the practitioner should measure for and adjust the instrument himself to his patient. This implies naturally a sound knowledge of the type of truss required, of the method of measurement, of the proper manufacture, and of anatomy for adjustment. It is for this reason that it is most desirable that all students should continue to be taught well the essentials concerning the modern treatment of herniae by trusses.

[The lecture was followed by a demonstration of trusses and their application to a living man.]

THE MECHANISM OF BLACKWATER FEVER AND CERTAIN ALLIED CONDITIONS.

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BLACKWATER FEVER is without doubt the most important and serious disease affecting Europeans in tropical countries; not even yellow fever can compare with it as regards mortality. It is difficult to overestimate the retarding influence of this infection on the development of our tropical possessions. Apart from the regrettable loss of men who are just beginning to render valuable services to their country, there is the depressing effect on the surviving European population in endemic areas. The fever is regarded with great dread by the laity, and is a cause of grave anxiety to medical practitioners where it exists.

The etiological theory which we now present is believed to be entirely new, but the evidence which we have obtained would seem to warrant our belief that it is correct.

DISTINCTIVE BIOLOGICAL FEATURES OF *P. falciparum*.

It is to-day generally agreed that blackwater fever arises mainly in the course of prolonged infection with *Plasmodium falciparum*. As there is no evidence that the malignant tertian parasite produces a toxin which differs from that of the other malaria parasites, we must seek for the explanation of this association between blackwater fever and *P. falciparum* in some biological factor other than toxin production.

The outstanding differences between *P. falciparum* and the other malaria parasites are that the former sporulates not in the peripheral blood but in the internal organs, and that the cells containing the sporulating forms adhere to each other and to the vessel walls. These phenomena were observed in the early work on the malaria parasites, and have been constantly recognized. Marchiafava and Bignami,¹ in 1894, said of malignant tertian malaria, "Malignancy coincides with an exceptionally abundant quantity of parasitic forms, a quantity much more abundant—where the cases terminate fatally—in the blood of the viscera than in the blood of the finger." Christophers and Bentley² noted that it was in infections by the malignant parasite that the organs were found to be most actively engaged in holding up the infective red cells, the very perniciousness of infections by this parasite being suggestively associated with such an action. Three observations serve to explain this tendency of the malignant tertian parasite to accumulate in the internal organs. Marchiafava and Bignami³ drew attention to the fact that corpuscles infected with malignant parasites, especially of the adult form, have lost their elasticity, and consequently resist the change of shape necessary for their passage through the capillaries, an observation which was again made by Bass.⁴ Next Thomson and Thomson⁵ recorded and illustrated marked clumping of the infected red cells in culture during all stages of sporulation of *P. falciparum*, whereas no tendency to clumping occurred in cultures of *P. vivax*. The two observations so far mentioned would account for the accumulation of the sporulating forms of *P. falciparum* in the capillaries of any part of the body, but not necessarily in the internal organs. Their predilection for the internal organs was explained by Bass, who showed that they lodge in those capillaries where the current is weakest or where slight obstruction is produced by the protrusion of endothelial cells inward. The commonest and most important site of this massing of infected cells is the spleen, though the bone marrow and other organs may be similarly affected. We may allude here to the massive infections found by Clarke⁶ in the placentas of parturient women, even in cases where the peripheral blood was free from parasites, a finding which was confirmed by Blacklock and Gordon.⁷

We are convinced that the association between blackwater fever and *P. falciparum* must depend on these distinctive biological characters of this parasite; we hope also to make it clear that as a result of these very characters of the parasite the condition known clinically as blackwater fever has fundamental affinities with several other forms of haemoglobinuria and haemoglobinaemia.

DEFICIENT OXYGENATION IN THE HAEMOGLOBINURIAS AND HAEMOGLOBINAEMIAS.

We have selected for comparison with blackwater fever a group of haemoglobinurias and haemoglobinaemias which seem at first sight to have little relationship to each other, but which on closer investigation reveal notable features in common. The group includes: haemoglobinuria in pernicious anaemia complicated by venous thrombosis; haemoglobinuria in Raynaud's disease; haemoglobinaemia in dogs as a result of exercise; haemoglobinuria in man from marching; and myoglobinuria in horses. One feature common to all these conditions is the existence in them of a state which results in deficient oxygenation, either local or general; the manner in which this state is brought about may be considered under the various diseases.

1. *Blackwater Fever*.—In an earlier paragraph we have described how the sporulating malignant tertian parasites adhere to each other and to the vessel walls, forming large agglutinated masses in the internal organs. Deficient oxygenation naturally follows, and the pre-existing malarial anaemia accentuates this local oxygen deficiency.

2. *Pernicious Anaemia Complicated by Venous Thrombosis*.—Panton and others⁸ describe two cases of repeated haemoglobinuria in men who had a clinical condition and blood picture suggestive of pernicious anaemia, complicated by the presence of thrombosis of superficial veins. The existence of an oxygen want is inevitable in this combination of general anaemia and local stasis of blood, a condition which has a definite affinity with the conditions present in cases of blackwater fever.

3. *Raynaud's Disease*.—Haemoglobinuria is the most remarkable complication of this condition, and occurs in a considerable number of cases. As a rule the urinary changes are only met with during the existence of local cyanosis, and the attacks are more likely to come on when the patient is up and about; when the patient is put to bed the haemoglobinuria may cease; haemoglobinaemia has also been observed. In Raynaud's disease there is local deficiency of oxygen, brought about by spasm of the arterioles.

4. *Haemoglobinaemia in Dogs after Exercise*.—Hastings⁹ has described the frequent occurrence of haemoglobinaemia in untrained dogs which are subjected to running exercise.

5. *Haemoglobinuria from Marching*.—Stephens¹⁰ has collected the records of twenty-three cases of haemoglobinuria due to marching in otherwise normal persons. It seems legitimate to infer that this form of haemoglobinuria frequently occurs without being noted, because Feigl, in examining twenty-six persons after a long march, found haemoglobinuria in no fewer than eighteen, or about 70 per cent. of them.

6. *Myoglobinuria in Horses*.—Stephens also refers to the myoglobinuria which occurs in horses, long stabled on rich food, when they undergo sudden exposure to cold or exertion, either factor being said to suffice. As regards the untrained dogs mentioned above, there is clearly established in them an oxygen debt. It is similarly evident from the description of the cases of haemoglobinuria due to marching that, with one possible exception, sufficient exercise was taken to result in an oxygen debt; the exceptional case was that of a boy who also had marked postural albuminuria.

We have drawn attention to the fact that the members of the group have the state of anoxaemia in common; a difference between them lies in the manner in which this state is brought about. Whereas in blackwater fever the malignant tertian parasite plays an obviously important part, in the other diseases very different agencies are at work producing the same result.

If we next consider the effects which arise from deficient oxygenation in the animal body, we shall observe how these effects influence the production of haemolysis in the selected group, taking blackwater as our type.

DEFICIENT OXYGENATION AND LACTIC ACID FORMATION.

The Effects of Deficient Oxygenation.—Recent work by Hill, Long, Lupton, Furusawa, and others¹¹⁻¹⁴ has resulted in a considerable advance of knowledge of carbohydrate metabolism. Carbohydrate in the form of dextrose is brought by the blood stream and stored in the muscles as glycogen; the glycogen is converted into "lactacidogen," a hexose diphosphate, which is a compound of a monosaccharide and phosphoric acid. This is a readily dissociable compound which, on muscular contraction, is broken down into phosphoric acid and sarcolactic acid; the reaction is anaerobic. When the oxygen supply is sufficient one-quarter to one-sixth of the sarcolactic acid is oxidized and some of the chemical energy thus liberated is used to resynthesize the rest of the sarcolactic acid to lactacidogen. In excessive exercise the body is incapable of immediately supplying sufficient oxygen, and the lactic acid accumulates to a maximum of 0.45 per cent. in the muscles and 0.2 per cent. in the peripheral blood. The lactic acid produced is neutralized only slightly by the

carbonate of the plasma, the main reaction being with the sodium proteins, forming sodium lactate and an acid protein; the chief protein used for this purpose when lactic acid is liberated in the blood stream is haemoglobin. There is thus a definite acidosis in exercise, due to the presence of ionized protein. The metabolism of carbohydrate in the other tissues of the body also produces lactic acid as an intermediate stage, though possibly not by an identical mechanism.

It is very important to note that this cycle of carbohydrate transformation is a continuous one even in the normal resting state, when there is no visible evidence of muscular activity; it follows, therefore, that if for any reason there is a deficient supply of oxygen, lactic acid will accumulate. This has been demonstrated by Clausen,¹⁵ who noted a marked increase in the lactic acid content of the blood of adults with cardiac decompensation and infants with anhydraemia from diarrhoea, both being conditions causing anoxaemia by circulatory disturbance. Macleod¹⁶ produced a great excess of lactic acid in the blood of dogs by making them breathe an atmosphere deficient in oxygen.

The normal quantity of lactic acid in the blood of the resting individual is approximately 20 mg. per 100 c.cm.; the following table shows the effects produced by exercise and deficient oxygenation.

TABLE I.—Showing the Quantity of Lactic Acid in the Blood after Exercise and Anoxaemia.

Author.	Subject of Experiment.	Condition.	Lactic Acid mg. per 100 c.cm.
Hill, Long, Lupton (1924)	Normal individuals	Severe exercise	80-100
Hill, Long, Lupton (1924)	Trained athlete	Severe exercise	204
Clausen (1925)	Adult (human)	Cardiac decompensation	160
Clausen (1925)	Children	Anhydraemia	23-150
Macleod (1921)	Dogs	Atmosphere containing only 5.9% of oxygen	98
Macleod (1921)	Dogs	Extreme anoxaemia	123

The table illustrates how deficiency of oxygen from whatever cause always produces an excess of lactic acid in the blood. In view of the fact that all the haemoglobinurias and haemoglobinaemias which we have included in our group are associated with oxygen deficiency, we are driven to the conclusion that in each of them excess of lactic acid is produced.

That some normal product of body metabolism such as lactic acid is involved in the haemolytic process of blackwater fever appears probable from the facts which have been mentioned above. The etiological resemblance between blackwater fever and the other conditions in respect to anoxaemia has been shown. Now in certain of these latter conditions it is assured that the cause of the haemolysis is some natural product of the animal body; this is best seen in the experiments resulting in haemoglobinaemia in normal dogs and in the observations on haemoglobinuria in man caused by marching, where haemoglobinuria is induced simply by exercise. It appears, therefore, essential to investigate what haemolytic properties lactic acid possesses.

HAEMOLYTIC PROPERTIES OF LACTIC ACID.

In our first experiments we used a sample of commercial lactic acid which was in stock in the laboratory; this acid proved haemolytic up to 1 in 1,000, using a 10 per cent. cell suspension of normal human blood which had been defibrinated; the sodium and ammonium salts prepared from the acid proved non-haemolytic. We did not perform any animal experiments with these substances as the racemic form does not occur in the animal body. In our next series of experiments with lactic acid we used a sarcolactic acid which we ourselves prepared according to a textbook technique; this substance was discarded after several months' experimentation *in vitro* and *in vivo*, as it was then found that the presence of impurities in the acid

made the results of our experiments unreliable. We therefore obtained from Dr. Martindale a supply, as pure as possible, of sodium and ammonium dextralactate and also of dextralactic acid itself. The sodium and ammonium salts proved non-haemolytic, in any concentration possible in the human body, to human red cells *in vitro*. The acid proved highly haemolytic to suspensions of thrice-washed red human cells in saline solution—for example, complete haemolysis was obtained in a dilution of 1 in 600 and slight haemolysis in a dilution of 1 in 1,200, when a 10 per cent. suspension of cells was used. The use of suspensions of washed cells, although of value in demonstrating the presence of a haemolytic agent, is somewhat artificial in that it does not allow for the protective action of the plasma. We therefore tested the acid on blood approximating as nearly as possible to its normal condition, as in the following experiment.

Five cubic centimetres of blood were withdrawn from the vein of a healthy European into 0.5 c.cm. of 1 per cent. solution of sodium citrate in normal saline. A series of tubes was then put up, each containing 0.8 c.cm. of this blood and 0.2 c.cm. of a dilution of the acid; Table II shows the result of the experiment after three hours' incubation at 37° C.

TABLE II.—Showing the Haemolytic Effect of Sarcocollactic Acid on Human Blood.

0.2 c.cm. of Lactic acid, Strength.	Citrated human blood.	Final dilution of acid.	Haemolysis.
1 in 40 ...	0.8 c.cm.	1 in 200	++
1 in 80 ...	0.8 c.cm.	1 in 400	+
1 in 120 ...	0.8 c.cm.	1 in 600	0
1 in 160 ...	0.8 c.cm.	1 in 800	0
1 in 200 ...	0.8 c.cm.	1 in 1000	0
Saline control ...	0.8 c.cm.	—	0

From the *in vitro* experiments it appeared probable that if a concentration of 1 in 400 of sarcocollactic acid could be brought about in the blood of an animal haemolysis would result. Enormous quantities of sarcocollactic acid are produced in the animal body by exertion, but it is extremely difficult to approach such quantities by means of injection. The difficulty is that if strong solutions are injected there is a risk of killing the animal; if, on the other hand, dilute solutions are used, the bulk of the injection is so great that the process takes a long time to complete and the necessary haemolytic concentration is not attained. Table III shows the results of intravenous injections of various amounts and strengths of lactic acid; we have omitted three rabbits, two of which died immediately after intravenous injections of very strong solutions, while the other had haemoglobinuria after two injections, of which an uncertain amount was introduced into the vein, the rest passing subcutaneously. In none of the animals included in the table was any serious after-effect noted.

TABLE III.—Showing the Results of Intravenous Injection of Sarcocollactic Acid.

Animal used.	Strength of Sarcocollactic Acid.	Total volume injected.	Result.
Rabbit ...	5% ...	8.0 c.cm.	Haemoglobinuria.
Rabbit ...	4% ...	20.0 c.cm.	Haemoglobinuria.
Rabbit ...	3% ...	20.0 c.cm.	Haemoglobinaemia.
Dog ...	2% ...	26.5 c.cm.	Nil.
Rabbit ...	2% ...	20.0 c.cm.	Slight haemoglobinaemia.
Rabbit ...	2% ...	20.0 c.cm.	Nil.
Rabbit ...	2% ...	100.0 c.cm.	Haemoglobinaemia.
Rabbit ...	2% ...	9.0 c.cm.	Haemoglobinaemia.
Rabbit ...	1% ...	10.0 c.cm.	Nil.

In those cases where haemoglobinaemia alone resulted the bands of oxyhaemoglobin were found on spectroscopic examination. In the two rabbits in which haemoglobinuria developed the urine was alkaline, dark reddish-brown in colour, and contained a dark granular deposit; bands of oxyhaemoglobin were present. It will be observed in Table III that the injection of 100 c.cm. of 2 per cent. strength resulted in haemoglobinaemia only, whereas the injection of 20 c.cm. of 4 per cent. strength produced haemoglobinuria. We have evidence that the haemolysis in this last animal was not produced to any extent by the solution acting in its original strength. The evidence is derived from *in vitro* experiments, which showed that this strength of acid, acting on different volumes of blood, produced different results according to the final concentration. When this was greater than 1 per cent. oxyhaemoglobin was not formed, while when haemolysis ensued at weaker

concentrations oxyhaemoglobin was liberated. As from *in vitro* experiments the haemolytic titre was 1 in 400, or 0.25 per cent., it appears probable that the concentration of acid which was responsible for the haemolysis in the rabbits lay between 0.25 per cent. and 1 per cent. Thus sarcocollactic acid is haemolytic *in vitro*, and *in vivo* produces haemoglobinaemia and haemoglobinuria when injected in concentrations well borne by animals.

To summarize our results so far, we have shown that there exists between blackwater fever and certain allied conditions the common factor of deficient oxygenation; we have illustrated how this deficient oxygenation gives rise to the production of lactic acid; and finally we have shown that lactic acid is haemolytic *in vitro* and *in vivo* in doses well borne by the animals.

SUGGESTED CAUSE OF THE HAEMOLYSIS IN BLACKWATER FEVER.

The foregoing facts make it probable that lactic acid is the haemolytic agent responsible for the production of blackwater fever as well as for certain allied haemoglobinurias. The anaemia produced by chronic malignant malaria, the stasis in the circulation of such an organ as the spleen brought about by the agglutination of parasitized red cells, and the frequently observed venous thrombosis result in a considerable degree of local anoxaemia and lactic acid accumulation. Very relevant in this connexion is the haemolysis observed by Panski¹⁷ in the spleens of normal dogs three hours after ligation of the splenic vein.

If we now find that the main exciting causes of blackwater fever are such as will produce contraction of the spleen, already enlarged in volume and choked with parasitized red cells, we may conclude that the circulation in the spleen will be thereby still further impeded and that the local anoxaemia will be increased.

LACTIC ACID IN RELATION TO THE EXCITING CAUSES OF BLACKWATER FEVER.

The best record which we have obtained of the exciting causes in a long series of blackwater fever cases occurs in the medical and sanitary reports of the Protectorate of Uganda for the years 1919 to 1924. In the total of 327 cases of blackwater fever, no fewer than 214, or 65 per cent., were precipitated by either exertion or chill or by both combined. Now Barcroft¹⁸ has shown that the spleen contracts on exercise, even mild exercise reducing the size of the healthy spleen to one-half, while severe exercise causes it to contract to one-sixth of its normal volume. Secretion of adrenaline also causes it to contract, and for this reason we have a contraction in chill comparable to that which results from exercise. Hoskins and Lee Gunning¹⁹ showed that adrenaline causes a brief dilatation followed by contraction of the spleen, and the work of Cramer²⁰ proved that exposure to cold is a powerful stimulus to the adrenal gland. The commonest exciting causes of blackwater fever are therefore exertion and chill, and each of these produces marked contraction of the spleen. Quinine is another exciting cause, and, according to the Uganda publication referred to above, it, either alone or in combination with some other factor, precipitated the disease in 41, or 13 per cent., of the cases. In many of the quinine attacks it is not easy to exclude some other exciting cause, such as exertion or chill; these additional causes are, however, excluded in certain cases. Thomson²¹ describes those which, whilst in hospital, repeatedly developed blackwater fever after quinine. Here the quinine concentration obtained in the blood could never be sufficient to exert a direct haemolytic action; the maximum concentration of quinine in the blood found by Ramsden, Lipkin, and Whitley²² after oral administration of large doses was 1 in 60,000, and *in vitro* very much greater concentrations than this have absolutely no haemolytic effect. What is evident, however, is that the drug, though non-haemolytic, would still exert its physiological action, demonstrated by Roth,²³ of causing active contraction of the spleen. The chief exciting causes of this fever—namely, exertion, chill, and quinine—have, therefore, this action in common, that they cause contraction of the spleen. The contraction of the spleen on

agglutinated masses of parasitized red cells accentuates, as we have said, the local anoxaemia; further production of lactic acid necessarily follows, especially on exertion, and finally the local concentration reaches such a level that haemolysis occurs. Leakage of haemoglobin into the portal circulation results as soon as haemolysis commences, and becomes pronounced when the circulation through the spleen is re-established.

We have described the conditions leading up to the haemoglobinuria of blackwater fever as occurring in the spleen, and probably in the majority of attacks this is correct. As evidence in favour of this being the case we may quote the following observations. Christophers and Bentley²⁴ noted that in all their twenty-seven cases of blackwater fever splenic enlargement was present; Barratt and Yorke²⁵ found that in their sixteen cases where record of the size of the spleen was kept, enlargement was present in fifteen, one case having a barely recognizable degree of haemoglobinuria without appreciable splenic enlargement; Thomson²⁶ observed marked enlargement of the spleen in all the eight cases which were examined *post mortem*. Barratt and Yorke further make the following significant statement: "The illness was severe in those attacks in which the enlargement of the spleen was greatest; in those in which enlargement was slight or not appreciable the attack may be described as mild, except in one case." The patient in this case died seven days after haemoglobinuria had ceased. That a similar process may go on in other organs is, however, probable; we have already mentioned the massive infection of the placenta in endemic areas where *P. falciparum* occurs. During labour the contractions of the uterus acting on vessels choked with sporulating parasites increase the existing local anoxaemia and prevent the oxidation of the lactic acid formed. For this reason haemoglobinuria during or as a result of labour might be expected to occur more readily in European women in an endemic area who have had chronic infection with malignant tertian parasites. In such cases where the taking of quinine has been very irregular or avoided entirely, the parasites multiply freely, the anaemia becomes progressively greater, and the spleen enlarges. Labour itself, with the excessive muscular contraction and exertion, acts as the exciting cause; in these cases a certain proportion of the haemoglobin to be disposed of is probably liberated in the uterine vessels. Thomson²⁷ gives records which are of great interest in this connexion; he notes that of the nine cases of blackwater observed by him in which no quinine had been taken, no fewer than five were precipitated by childbirth.

CLINICAL CONSIDERATIONS IN BLACKWATER FEVER.

1. *Typical Blackwater Fever.*—The mechanism of this has been described above.

2. *Quinine Haemoglobinuria.*—This is a condition in which a dose of quinine, whatever the amount, will with some certainty induce a transient attack of haemoglobinuria in a susceptible person; there are innumerable records of this in the literature.

3. *Transient Haemoglobinuria following a Chill or Exertion.*—Parsons and Forbes²⁸ give their observations on forty-six cases of blackwater fever; they noted that the majority of cases presented a very transient haemoglobinuria following exposure to cold or fatigue. These conditions of transient haemoglobinuria due to quinine, chill, or exertion could all be produced by the contraction of a spleen in which haemolysis had been slowly taking place, with the consequent expulsion of the contained haemoglobin into the circulation, from which it is quickly eliminated.

We may distinguish from typical blackwater fever, in mechanism if not in results, those occasional cases in which numerous parasites are present in the blood throughout the attacks. The continued presence of large numbers of parasites in itself suggests a mechanism somewhat different from that which occurs normally in blackwater fever. The most probable explanation of the haemoglobinuria in such cases is that it is largely due to direct destruction of infected red cells by the parasite during schizogony, a condition comparable rather with piro-

plasmosis of dogs than blackwater fever in man. Such a form of haemoglobinuria might occur equally well in infection with other forms of malaria parasite.

SOME PROBLEMS IN CONNEXION WITH BLACKWATER FEVER.

1. *The Length of Residence.*—Much difficulty has been experienced in giving an explanation to account for the period which elapses before the first attack of blackwater fever comes on, and also for the relative immunity which seems to develop after some years' residence in the endemic areas. Table IV is an extract from a table given by Stephens²⁹ showing that the majority of attacks occur after six months' residence and before the end of five years' residence.

TABLE IV.—Showing the Effect of Length of Residence on the Onset of Blackwater Fever.

Length of Residence.	No. of Cases.	Per cent.
Six months	76	7.2
One year	224	21.3
Two years	346	33.0
Three years	261	24.9
Four years	102	9.7
Five years	42	4.0
Later	75	7.1

As regards the relative freedom from attack in the first six months we believe that the explanation is to be found in the length of time which is required before the malaria parasite usually produces a marked degree of anaemia, and also in the length of time that it takes for the spleen to enlarge. If our theory of the common mechanism of blackwater fever is correct, we should not anticipate that the contraction of a small spleen would result in the expulsion of sufficient free haemoglobin to cause haemoglobinuria. During the pre-blackwater fever period, however, it is probable that many subliminal attacks occur. As regards the relative freedom in after years, it may be explained on the ground that after several years of chronic malaria the spleen becomes fibrosed, and, in this state, is less capable of contraction; this, together with the acquired tolerance to the malaria parasite, would explain the relative immunity of old residents in an endemic area.

2. *The Danger of Moving Blackwater Fever Cases.*—It has long been recognized that there is a grave risk in moving a case of blackwater fever even with all possible precautions, and even for short journeys; no satisfactory reason for this has been offered. It appears to us that an explanation is available as a result of our observations recorded above. The blackwater fever patient is extremely anaemic, and has already had a sufficient degree of anoxaemia to result in haemolysis; he will, especially if he is suffering from pain, make the greatest possible efforts to avoid the discomfort to which he is subjected in transit, and in so doing he will contract his muscles continually, thus producing lactic acid in amounts which cannot be properly oxidized. It is to this lactic acid production that we attribute the relapses which occur so frequently when blackwater fever patients are moved.

3. *Jaundice in Blackwater Fever.*—The occurrence of early and often intense jaundice of a degree such as does not appear in paroxysmal haemoglobinuria, nor after the injection of even large quantities of haemoglobin into animals, can be explained by the site of the injection, or of the haemolysis. In blackwater fever the haemoglobin is usually delivered directly into the portal system, and thus reaches the liver in a concentrated form, whereas in paroxysmal and experimental haemoglobinuria the haemoglobin is liberated in the peripheral blood and is considerably diluted before reaching the liver. Pearce and others³⁰ have shown experimentally that the injection of haemoglobin into the portal system produces less frequent and less marked haemoglobinuria coupled with more frequent and intense jaundice than a similar injection into a systemic vein; the site of haemolysis is therefore the important factor in the production of jaundice in blackwater fever.

SUMMARY.

1. Points of resemblance between blackwater fever and certain other haemoglobinurias and haemoglobinaemias are indicated.

2. These points include the presence of an anoxaemic state, and a resultant increase in sarcolactic acid either locally or generally.

3. We produce evidence from experiments, both *in vitro* and *in vivo*, that sarcolactic acid is haemolytic—in the former case to whole human blood, and in the latter to whole animal blood.

4. Intravenous injections of sarcolactic acid into rabbits have produced haemoglobinaemia and haemoglobinuria, followed by recovery of the animals.

5. On the evidence brought forward by us, we conclude that sarcolactic acid is the causal agent in the production of the haemolysis in blackwater fever and these haemoglobinurias.

6. The etiology of various types, symptoms, and complications of blackwater fever is discussed in the light of this mechanism.

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THE GUILLOTINE AND ETHYL CHLORIDE.

TEAM WORK FOR THE REMOVAL OF TONSILS AND ADENOIDS.

BY

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THE following observations and description of methods for the removal of the tonsils (with the guillotine) and of adenoids (with the curette) are based on experience gathered from 13,500 cases operated on at Queen Mary's Hospital, Stratford.

The ages of the majority of the patients ranged from 1 to 15 years. The operations were performed by special team work in sessions of twenty-five to thirty patients; and the method has permitted of thirty patients being operated on in one hour. The efficiency of this team work necessitated two operating tables and a movable instrument table; four sets of instruments at least; a sister, a nurse, and a porter who is experienced in carrying in the theatre; one nurse in the waiting room; two nurses in the recovery room for the first twenty cases, with an additional nurse for every ten extra cases or part of ten.

Ethyl chloride was used in the entire series of cases, except for an occasional open ether for instructional purposes in operating. There has been one death. The patient, a girl of 19, was acutely poisoned by the ethyl chloride at the commencement of induction.

For descriptive purposes our observations will be made under the headings: Pre-operative, Operative, and Post-operative.

PRE-OPERATIVE CONSIDERATIONS.

Cases for operation are divisible into those with definite indications and those with indefinite indications.

Cases with Definite Indications.—These are the ordinary textbook cases: discharging ears, due to tympanic infection only, not complicated by attic disease, chronic mastoiditis, granular mucous membrane in the middle ear, aural polypus, enlarged tonsillar gland which is found at the anterior border of the sterno-mastoid about half an inch below a line drawn backwards along the lower border of the jaw, attacks of earache, deafness, frequent colds, snoring, and mouth breathing. The adenoid facies is becoming a rarity, and rightly, because its development signifies that the case has waited too long and changes have occurred in the shape of the palate, which becomes raised in the form of a high arch, thus causing deformity of the nasal septum above and crowding of the teeth below. Even in infants up to 6 months of age an indication that the adenoid tissue in the nasopharynx is excessive in amount is given by the state of the hair at the back of the head. The anoxaemia produced causes restlessness during sleep; as a result the hair is often worn off the occipital region, leaving a thin patch.

Cases with Indefinite Indications.—Many children are sent up for operation because they are not sufficiently bright, or they are not putting on weight, or they are too sallow and hollow-eyed.

Acute Tonsillitis.—In order to increase the percentage of tonsils completely enucleated by guillotine it is advisable not to operate within one month of an acute attack of tonsillitis, and preferably not for six to eight weeks. The amount of induration at the base of the tonsils is such as to make this region so ligneous that great difficulty arises in dislocating a tonsil from its bed, a process essential for its complete removal.

Nasal Diphtheria.—When examining large numbers of children nasal diphtheria is occasionally observed, usually in cases least expected. One case seen with a typical membranous rhinitis was brought up because the boy had been hit on the nose with a football the week before. One point in aid of diagnosis of this disease is that with few exceptions a florid red excoriated area of skin can be seen on the upper lip close to the columella of the septum. A typical membranous rhinitis is less common than an acute catarrhal rhinitis plus this excoriated area.

Patients selected for operation are given a list of instructions to follow; preparatory to operation and on the morning of operation the temperature is taken, the urine examined, and the chest auscultated. The urines are tested for albumin and sugar in groups of five, individual testing being carried out where any group shows a positive. About 6 or 7 per cent. of children show some transitory albuminuria, which may possibly be due to the preparatory starvation.

OPERATIVE TECHNIQUE.

The Anaesthetic.

As already stated, ethyl chloride was used except in a very few cases. Throughout the whole series the same inhaler was used, and the same brand of anaesthetic as supplied by Messrs. Duncan Flockhart. The one thing materially altered after the first few hundred cases was the method of administration.

The inhaler employed is called the "Queen's"; it was first used at the Queen's Hospital for Children, Hackney Road. It consists of a rubber bag, an L-shaped junction, and a facepiece. A strong red rubber bag is preferred for its durability and economy. The L-shaped junction has a movable device which permits of an easy regulation of air and anaesthetic, and is situated on the upper surface of the horizontal limb of the junction. Close to it, but nearer the bag, is the mouth of a tube which carries the ethyl chloride into the rubber bag, where it is soaked up by a swab of gauze held in forceps at the end of the tube. This soaked gauze is prevented from damaging the rubber bag by a wire cage. The