A CASE OF ACUTE DIABETES.

WITH COMMENTS, ESPECIALLY IN REGARD TO ACIDOSIS.

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THE following are the main facts of the case upon which I propose to comment.

Notes of the Case by Mr. C. H. COMERFORD.—The patient, a boy aged 7 years, was admitted on Jan. 4th, 1916, and remained in hospital only one week, when his parents took him home fearing he was about to die. He was a gentle, quiet child, very thin, and wore a wan and apathetic expression, although his complexion was good and his eyes fairly bright. His parents stated that he was naturally healthy, and had had no previous illness to speak of. He was apparently quite well up to Christmas-time, 1915. It was then noticed that he had to get up three or four times a night to pass urine. There was marked thirst, his appetite became inordinate, while his strength and energy languished. He lay in bed almost motionless, took no interest in his surroundings, the upper eyelids drooped, and he slept a good deal. Emaciation was very marked. The skin was rather dark on the legs and its surface dry and rough, owing to minute horny accumulations at the hair follicles. No complaint of itchiness, no eruption on the skin, and no oedema of the ankles. The tongue was very red and the lips were dry and cracked, while the teeth and gums were normal. Bowels costive, motions large. No physical signs of disease in thorax or abdomen. Cardiac sounds normal; pulse varied from 80 to 100; temperature subnormal. No odour from the breath. As a rule, the patient answered questions intelligently, but the nurse reported that his mind sometimes rambled. The plantar reflex and the knee-jerk were completely abolished, and the cremasteric reflex, usually so active in a young boy, was poorly marked. His appetite was voracious and his thirst excessive and unceasing. Micturition very frequent, and he sometimes passed as much as six pints of urine in the 24 hours; on one day four pints in four hours. Urine always odourless, limpid, and brilliant, showing greenish fluorescence. There was never but the slightest trace of any sediment or deposit whatsoever. No crystals visible under the microscope. The specific gravity varied from 1030 to 1050. Reaction acid. Albuminuria was never found. Sugar very abundant, up to 8.33 per cent. (Dr. Alfred Scott.) By Roberts's differential density method I found from one sample 30 grs. in 1 fl. oz. Specific rotation by polarimeter was 6.25 (Mr. Fearon) corresponding to about 9 per cent. sugar; abundant precipitate with phenylhydrazine test. The urea content was not determined. No crystals of uric acid could be obtained by the addition of HCl either to the fresh or concentrated urine. Mr. Fearon failed to find evidence of the production of α -crotonic acid after distillation from sulphuric acid. So rich was the urine in lime that it became opaque white after addition of acetic acid and ammonium oxalate, and there was considerable opacity of phosphates after addition of liq. potassæ. It yielded Gerhardt's reaction with ferric chloride, and developed a fine purple with sodium nitro-prusside and liquor ammoniac.

The boy's eyes were not specially examined, but there was nothing obviously wrong, and vision was good.

Blood examination by Dr. J. T. WIGHAM.—Red cells, 5,250,000; white cells, 5200; hæmoglobin, 80 per cent. Blood smear appeared normal with due proportion of white cells. Some blood was drawn off and ammonium oxalate added to prevent clotting. The drawn blood separated into two strata. The lower stratum was opaque, dark red. The upper stratum was opalescent, bright red. Both in the fresh blood and in the upper layer of the drawn blood I observed under the microscope numerous spherical refractile globules of various sizes. These stained well with Sudan III., so there was well-marked lipæmia. Dr. Alfred Scott confirmed this observation, using Scarlet R. as a stain. Blood normally contains from 0.2 to 0.3 per cent. of fat.

Diabetes mellitus is uncommon in young children and notoriously runs a more disastrous course than in adults, and especially than cases in middle and elderly life. As v. Noorden puts it: "Infantile diabetes knows no mercy."

Strictly speaking, both glycosuria (or glucosuria) and albuminuria should be regarded not as altogether new events, but as exaggerations of a physiological condition. For it is generally conceded that in healthy normal urine occur traces

of (a) proteins and (b) sugar, or at least reducing carbohydrates (about 0.01 per cent.). The glucose content of normal blood is about 0.05 to 0.15 per cent. In diabetic blood Gardner and Maclean found an average of 0.22 per cent. Even after a prolonged fast sugar is never absent from the blood of the normal animal.

In this communication I restrict my remarks to a few points, and will not attempt a comprehensive survey of a deadly and mysterious affection.

The etymology of the term diabetes has been referred to the Greek word *διαβήτης*, a siphon. The word also signifies a pair of compasses. The latter is the more plausible idea, derived from the verb *διαβαίνω* to straddle, connoting the necessity for frequent micturition. Mr. Kennedy, F.T.C.D., informs me that the prefix *δια*, in Greek, corresponds to *dis*, in Latin, and signifies *separation*.

Nearly 250 years have passed since the sweet taste of diabetic urine was first noticed in Europe by Dr. Thomas Willis (1674). But according to the Ayur Veda (500 A.D.) the saccharine nature of diabetic urine had been known to Hindu physicians from remote times, and in the fifteenth century a disease was described characterised by "honey urine." In 1815 the French chemist Chevreul showed that diabetic sugar closely resembled grape sugar, and in 1848 Claude Bernard proclaimed his fundamental discovery that animals could manufacture sugar, and some years later he demonstrated the glycogenic function of the liver. From that time on the study of diabetes was removed from empiricism and was firmly based upon physiology.

Let us start with a definition of diabetes. Osler's definition in the eighth edition of his "Practice of Medicine," p. 426, runs thus: "A syndrome due to disturbance in the carbohydrate metabolism from various causes, in which sugar appears in the urine, either as a slight and transient condition (glycosuria), or, as a more severe form, associated with thirst, polyuria, wasting, and imperfect oxidation of the fats (diabetes)." In his seventh edition a simpler and better definition was given. I would formulate the definition thus: "Diabetes mellitus is a disease characterised by increased glycohæmia, and by persistent excretion in the urine of sugars derived from faulty metabolism of imperfectly known, and probably various, kinds." This definition is, I think, more concise and more exact, and leaves open for discussion the thesis that there may be several types of diabetes mellitus. Moreover, the definition as stated excludes (a) dietetic glycosuria; (b) transient glycosuria of corpulent or gouty people (sometimes noticeable only after a principal meal); (c) lactosuria of pregnancy, the puerperal state, and in early infancy; (d) phloridzin glycosuria (here there is no increased glycæmia); (e) adrenalin glycosuria; and (f) experimental pancreatic glycosuria—i.e., complete extirpation of the pancreas. One-fifty-fifth part of the organ suffices to prevent the development of the symptoms, which show that there is a profound relation between the pancreas and carbohydrate metabolism. The glucose content of the blood may be raised to 0.8 per cent.

The word *sugars* is advisedly used in the plural, for, as a matter of fact, it is well established that several sugars may be concerned in the pathology of diabetes. They fall into three groups: 1. Those with 6 atoms of carbon in the molecule—hexoses, $C_6H_{12}O_6$, or monosaccharides; glucose (dextrose), an aldose; levulose (fructose), a ketose. Levulose may occur along with glucose, and Seegen and others have recorded cases of diabetes where the urine contained only levulose and no grape sugar. The use of starchy foods increased the amount of levulose (Laache, *Harn-Analyse*, 1885). 2. Those with 12 atoms of carbon—bioses, or di-saccharides ($C_{12}H_{22}O_{11}$). Here we meet with the two isomers: Maltose (sometimes concurs with glucose); Lactose. Cane sugar (sucrose) never occurs pathologically. 3. Those with 5 atoms of carbon—pentoses, giving rise to pentosuria ($C_5H_{10}O_5$). It has been shown that, owing to differences in stereo-chemical configuration, only sugars with C_3 , C_6 , and C_9 atoms of carbon in the molecule are capable of direct fermentation by yeast, and of these only the C_6 group is of interest to the clinical physician. Among the hexoses only the four naturally occurring sugars—viz., *d*-galactose, *d*-mannose, *d*-glucose, and *d*-fructose—are directly fermentable. This is a fact of extreme interest. It follows, therefore, that pentoses are not attacked by yeast. If co-existent with hexoses—e.g., glucose, a pentose could be detected in urine after

fermentation with yeast, which destroys only the hexose. After complete fermentation I tested in the foregoing case the urine for pentose by the orcin and phloroglucin tests with negative results. It remains, of course, true that the predominant, and usually the only, sugar present in diabetic urine is glucose.

Notwithstanding a vast expenditure of patient toil and chemical skill, the etiology and pathogeny of diabetes still remain obscure, and I will not spend time upon this intricate, albeit fascinating, inquiry. It is not unlikely to prove true that the prime factors underlying the development of glycosuria are connected with disturbances in the balance of the internal secretions of the body. Neither do I propose to touch upon the morbid anatomy of fatal cases of diabetes upon which we have little satisfactory or illuminating knowledge. I propose to restrict my observations mainly to clinical symptoms and to the conditions observed in the urine. The important subject of treatment must be entirely passed over.

What are the obtrusive symptoms of a fully declared case of diabetes in a young subject? Are they not these? The patient is (a) thirsty (polydipsia); (b) leaky (polyuria); (c) emaciated (autophagia); (d) hungry (polyphagia—bulimia); (e) saccharine (glycosuria).

We next inquire what are the chief dangers of diabetes. They fall under these heads (cf. v. Noorden: Diabetes Mellitus, 1906):—

DANGERS.	RESULTS.
(a) Carbohydrate deficiency.	Lowered nutrition. Carbohydrates are even more essential than fats as sources of body energy.
(b) Degenerative changes in the nuclein substances of cells.	Increased excretion of uric acid, and xanthin bases.
(c) Abnormal production of acids; derived mainly from breakdown of fats, which are the reserve fund of fuel for active cells.	β -oxybutyric acid. Acetoacetic (diacetic) acid. Coma.
(d) Other products of abnormal metabolism.	Excess of acetone. Increased excretion of lime in the urine, and also of phosphates.
(e) Diminished resistance to intercurrent diseases. Increased vulnerability of skin, &c.	Tuberculosis. Pneumonia. Various affections of the skin.
(f) Chronic degenerative and inflammatory processes in tissues, especially the vascular and nervous systems.	Arterio-sclerosis. Gangrene. Neuralgia. Neuritis. Ocular affections. Albuminuria.

Perhaps the most noteworthy fact in the pathology of diabetes is the wide sweep of changes drawn into the net of the poison or poisons which circulate in the blood and tissues. No part of the body is exempt. From the crown of the head to the tips of the toes there are proofs of ubiquitous mischief-making. Still, it is plain that the most important and familiar clinical symptoms hinge upon perverted metabolism of two groups of foodstuffs—viz., the carbohydrates and the fats, upon which I will make some brief remarks.

Carbohydrates.—A due utilisation of carbohydrate is of supreme importance to the welfare of the body, and it is, moreover, essential to the maintenance of nitrogen equilibrium, for carbohydrates are *sparers of protein*. When the metabolism of carbohydrate is interfered with by complete removal of the pancreas there is a very great rise in the breakdown of body-protein, as is evidenced by the increased output of nitrogen. So that if the tissues of an animal cannot get or utilise carbohydrate directly, they strive to get it willy-nilly from protein, for the cells must and will have carbohydrate food at any price. (Falta, Grote, and Staehelin, quoted by Cathcart, "The Physiology of Protein Metabolism," 1912.)

As a practical side-issue in therapeutics, I may point out that Shaffer and Coleman have clearly demonstrated that the "toxic" destruction of body-protein in fevers may be largely prevented by securing the intake of carbohydrate food. This is highly important in the rational treatment of enteric fever, in which disease I have long been convinced that immense mischief is done by the fetish of an exclusively milk diet. The observations of botanical physiologists also support this contention. For example, it has been demonstrated by Hansteen and others that the presence of carbohydrate is absolutely essential before protein synthesis can take place in plants.

It is time now to inquire how stands our knowledge of the metabolism of carbohydrates and fats. If a lump of starch, sugar, or fat respectively is thrown into the fire it is certain that the ultimate and final products of combustion of all

three are the same—viz., CO_2 and H_2O . Expressed in symbols we have:—

Or, physiologically stated, the respiratory quotient is 1; for $\frac{6\text{CO}_2}{6\text{O}_2} = 1$.

But a physiologist or a physician wants to know more than this. He asks, What are the intermediate stages passed through, and whereabouts are breaks or modifications in the sequence of events to be expected or looked for?

The knowledge we possess as to the metabolism of carbohydrates is due mainly to the work of Embden and Dakin, and their associates. It is summarised by Bayliss as follows ("Principles of General Physiology," 1915):—

Most of these reactions are reversible, as shown by the single-headed arrows, and have been experimentally demonstrated as possible and probable steps. The chemical symbolism of the above transformations is not very difficult to follow, but I will not dwell upon it now.

Fats.—From a clinical point of view, and especially as regards the prognosis of a case of diabetes, the metabolism of fats is even more interesting than the carbohydrate changes. For mainly from fats are derived the group of bodies usually known by the unsatisfactory title of the "acetone bodies"—viz., oxybutyric acid, acetoacetic (diacetic) acid, and acetone. Unfortunately, our knowledge of the stages of fat metabolism is extremely deficient and we are sorely in need of more light. The chemical processes involved in the utilisation of fat are not sufficiently understood to enable one to draw up a table such as that given for carbohydrate.

In diabetes it has been shown that fats may and do break down into less complex acids—e.g., oxybutyric and acetoacetic acids, together with acetone, even when the diet is free from carbohydrate, and is formed exclusively of fat and protein. In the normal organism, an exclusively fatty diet, continued for some days, has been found to give rise to large quantities of these partially oxidised products (Bayliss). In short, the output of the "acetone bodies" affords us practically the only clue to the faulty metabolism of fat (Lang, *Biochem. Journ.*, December, 1915).

Acidosis.

Strictly speaking, any condition in which there is an excessive production of acid radicals can be referred to as acidosis. In rheumatic fever, for example, the urine is strongly acid, and often so persists in spite of the ingestion of considerable amounts of alkalies. There is no proof that the acidosis of fevers gives rise to recognisable clinical symptoms, and the amount of acids so formed is relatively trivial compared with their excretion in diabetes mellitus (Foster).

So far back as 1854 Sir Henry Marsh, of Dublin, referred to death in coma as a sequel of diabetes.¹ The view that some of the worst results of diabetes, notably the liability to sudden and fatal coma, are due to the accumulation

¹ Dublin Quarterly Journal, 1854.

⁴ Kennaway: Some Notes on the Excretion of Acetone Bodies, *Guy's Hospital Reports*, 1913, vol. lxvii. (A lucid and excellent paper.)

of by enzyme action, and that the trend of the reaction depends, among other conditions, upon the oxygen-supply. Much confusion has arisen from ignorance of the fact, first stated by Legal and established by Hurltley,⁷ that (Le Nobel's) Rothera's test with sodium nitroprusside and ammonia is given *both* by acetone and acetoacetic acid, and is about 20 times as delicate in regard to the latter. This difference in sensitiveness enables one to form a better idea of the amount of acetoacetic acid present (Kennaway). The test is wrongly fixed in the text-books as one for acetone only. A urine containing 0.01 per cent. acetoacetic acid and no acetone at all will fail to give the ferric chloride colour, while it still reacts to Rothera's test (Kennaway).

Furthermore, it can be laid down that the presence in the urine of acetone and oxybutyric acid is by no means characteristic of diabetes. Oxybutyric acid has been detected in the urine in a number of diverse conditions. Dr. Foster⁸ gives a striking experiment in proof of this. Several years ago when fasting was in vogue as a cure for all ills a normal man abstained from all food for five days. The urine was collected by Dr. Foster during the fourth day of the fast. The analysis gave:—

Amount.	Total N.	NH ₃ -N.	Acetone and diacetic acid.	β-oxybutyric acid.
1410 c.c.	11.42 grm.	1.09 grm. (9.6 %)	0.475 grm.	0.819 grm.

The grade of acidosis represented here is comparable to that found in mild cases of acidosis with diabetes and was induced in this case purely by abstinence from food. In truth, both the fasting man and the acute diabetic are self-cannibals. Any decrease in the alkali value (or relative increase of acidity) of the blood renders the blood less able to retain CO₂, and upon this follows a decrease in the CO₂ content of the blood. The composition of "alveolar air" in the lungs can be measured by the method of Haldane and Priestley.⁹ Consequently it would appear that the most scientific method of noting the degree of acidosis in the body consists in determination of the alveolar CO₂ of the lungs, and further observations are most desirable. Normal blood is very near the neutral point in reaction.

The organism possesses two main lines of defence against acidosis: (a) The fixed basic radicals, potassium and sodium; (b) the neutralising capacities for bases of acetoacetic acid and β-oxybutyric acid are practically identical for their molecular weights differ by less than 2 per cent. (Kennaway). If these bases are not equal to the task an increased amount of ammonia is provided, some of the N-excretion being switched off the normal path of excretion in the form of urea. Hence it follows that increased excretion of ammonia in the urine is a rough index of the degree of acidosis, and this has been shown to be the case in diabetes.

Foster¹⁰ further points out that there are two sources of weakness in the current acidosis theory of diabetic coma. Now one consideration that throws doubt upon the theory is this. The acids concerned occur, it must be presumed, not as free acids, but as salts, in combination with Na, K, ammonia. Sodium is the predominant base. The second weakness in the theory is that the blood in cases of diabetic coma does not invariably show preponderance of hydrogen ions. The blood may *not* be less "alkaline" than normal.

Of 11 cases examined by the electro-chemical method¹¹ Rolly found the hydrogen ions increased in only three. It is impossible to determine the true *hydrogen ion concentration of the blood* in any other way.¹² So that if further investigations substantiate Rolly's observations some changes in our conception of coma will be imperative. There is no evidence that either oxybutyric acid or diacetic acid exercise any specific toxic action apart from their acidic character. At present all we are entitled to say is that coma may come about by disturbance of the normal delicate adjustment of acid and basic radicals in the blood and tissues without postulating an excess of hydrogen ions in the blood.

Summary.

The foregoing inquiry appears to me to justify the following propositions:—

1. There is no simple direct test for oxybutyric acid at our disposal. Its detection can only be effected indirectly. Barium oxybutyrate forms long needle-shaped crystals (W. Caldwell) which are doubly refracting.

2. Neither oxybutyric acid nor acetone gives any colour reaction with ferric chloride. Oxybutyric acid has no reactions in common with acetoacetic acid. Hurltley's method for its quantitative determination by extraction with ether and estimation by titration and optical rotation is described in Plimmer (loc. cit., p. 597).

3. For acetoacetic acid¹³ three tests are available:—(a) Gerhardt's: Not very sensitive; hence much misapprehension. Failure of the ferric chloride reaction does not entitle one to state that acetoacetic acid is completely absent. (b) Rothera's test: Reacts with both acetone and acetoacetic acid. The latter is more sensitive to the test than acetone, in the ratio 20:1. One part of acetoacetic acid in 400,000 gives the reaction in five minutes. (c) Riegler's test: Differentiates acetone and acetoacetic acid. Method of applying the test: 10 c.c. of urine are acidified with five drops of 30 per cent. acetic acid, and five drops of Lugol's iodine solution are added. This mixture is shaken with 2 or 3 c.c. of chloroform. No colour appears if acetoacetic acid be present (Plimmer).

I have no experience of Arnold's test (para-amino-acetophenone) and little of Hurltley's purple test (iso-nitroso-acetone).¹⁴ They are more complicated and appear to be scarcely necessary. Plimmer, however,¹⁵ considers that Hurltley's reaction is very useful for gauging the amount of acetoacetic acid in a solution or in urine.

4. Acetone does not respond either to Gerhardt's or Riegler's test. Its reaction with Rothera's test is similar to that of acetoacetic acid, but is less sensitive. The sensitiveness of Rothera's test is increased by the addition of a solid ammonium salt (sulphate or chloride). The best way of employing it is this: Over a layer of the salt the urine is floated, and then tested as usual with nitroprusside and ammonia. I can confirm the value of this modification. I found that a specimen of diabetic urine preserved for nearly four weeks still gave a distinct red with FeCl₃. When diluted to 1 in 10 it scarcely reacted to the iron test. It failed to respond to Lugol's test, or to Le Nobel's (Rothera's) test until layered over solid (NH₄)₂SO₄, when a bright purple-red zone developed. It is stated in Neubauer-Huppert¹⁶ that acetoacetic acid disappears from urine at latest in 48 hours.

5. The amount of acetoacetic acid in urine is usually considerably greater than that of acetone—viz., from 2 to 10 times as much (Plimmer). There are two sources of acetoacetic acid in the urine: (a) preformed; (b) derived from intravesical decomposition of oxybutyric acid.

6. There is no simple and reliable test at present known for the detection in urine of small amounts of acetone in association with acetoacetic acid.¹⁷ Many data published in connexion with acetonuria are vitiated by ignorance of this fact. Scott-Wilson's method of detecting and estimating acetone alone by conversion into a keto-mercury-cyanide precipitate is described in Plimmer (p. 592).

7. Rothera's test differentiates acetone from creatinin. Creatinin reacts with sodium nitroprusside and either liquor potassæ (sodæ) or liquor ammoniæ. Acetone reacts only with nitroprusside and liquor ammoniæ.

8. The term "acetone bodies" (or "acetonuria") is not a happy one, for it lays stress on the least important member of the triad. Since acetone alone is not infrequently met with in urine, perhaps it would be well to indicate that fact by *acetonuria*, and to use the term *acetouria* for the cases in which acetoacetic acid occurs.

¹³ I am indebted to Professor W. Caldwell for a specimen of ethyl-acetoacetate which answers admirably for checking the tests.

¹⁴ Cf. Kennaway and Hurltley, loc. cit.

¹⁵ Pract. Organic Chem., p. 122.

¹⁶ Analyse des Harns, I., 268.

¹⁷ Frommer claims that his test with solid caustic soda and salicylaldehyde (purple-red) is specific for acetone only, but according to Bohrisch acetoacetic acid also responds. (Neubauer-Huppert, Analyse des Harns, 11te Aufl., 1910.)

⁷ THE LANCET, April 25th, 1913, p. 1160.

⁸ Diabetes Mellitus, 1915, p. 137.

⁹ This method is described and illustrated in Barcroft's valuable book, the Respiratory Function of the Blood, Cambridge, 1914, p. 309.

¹⁰ Loc. cit.

¹¹ Bayliss: General Physiology, p. 190.

¹² Münch. Med. Wochenschr., 1912, vol. lix., p. 1201.

9. The theory of "acidosis" is still incomplete. The modes of origin of "acetonuria" are complex, and are largely influenced by the amount of carbohydrate food assimilated.

10. For the solution of such difficult problems the coöperation of clinical physicians and experts in organic chemistry is essential.

Appendix.

Examples of errors and inaccuracies culled from textbooks on medicine and on urinary analysis.

1. Acetone gives a red colour with ferric chloride. This error occurs in Fagge, "Practice of Medicine," edited by Pye-Smith, 1888; and also in Roberts's "Treatise on Urinary and Renal Diseases," fourth edition, 1885. Gerhardt's test for acetoacetic acid was described in 1865.

2. Other substances (than acetoacetic acid)—e.g., formic, carbolic, and salicylic acids—give the same reaction in both fresh and previously boiled urine. For same read somewhat similar. No practised eye would confound the colours.

3. Both oxybutyric acid and acetoacetic acid react similarly with the ferric chloride test. This is not the case.

4. "Fehling's solution is reduced by acetone, but this test should be applied to the distillate from the urine." Acetone does not reduce the copper solution.

5. Rothera's nitroprusside test is true for acetone only. It is a much more sensitive test for acetoacetic acid.

6. Many drugs produce temporary diabetes. For diabetes read glycosuria.

7. "Large quantities of water are required (by the patient) to keep the sugar in solution, and for its excretion in the urine." Glucose is soluble in its own weight of water. The quantity of glucose in the blood of a severe case of diabetes is a fraction of 1 per cent.

Dublin.

TREATMENT OF SEPTIC WOUNDS, WITH SPECIAL REFERENCE TO THE USE OF SALICYLIC ACID.

NOTES BASED ON CASES AT THE MILITARY HOSPITAL, ENDELL STREET.

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THIS paper is based upon observations made upon approximately 1000 cases of septic wounds treated in the wards and operating theatres of the Military Hospital, Endell-street, during the period of six months from May to October, 1915. With the exception of a few cases from Gallipoli, all the men belonged to the British Expeditionary Force in France, and the majority were admitted to the hospital a few days after they were wounded.

While anaerobic infection was comparatively rare, septic infection was present to a varying degree in all the wounds. In order to test the effect of treatment on the bacterial growth in the wounds numerous agar cultures were made. The usual procedure has been to take cultures from the surface of the wounds, before and immediately after the dressings, each morning on successive days. After overnight incubation at 37° C. the relative number of colonies which developed on these cultures was noted. When wounds are irrigated with reagents such as hydrogen peroxide, weak solutions of perchloride of mercury, carbolic or boric acid lotion, there is often little difference to be noted in the number of colonies which develop on the cultures taken before and after the dressing or from day to day. For this reason the efficiency of many antiseptics when applied to wounds has been questioned, and it is evident that with reagents such as these the action of the lotion is often largely mechanical.

Many of the cases on admission were treated with hypertonic saline solution, either with continuous irrigation or with wet applications repeated two or three times a day. A preliminary test was made to determine the extent of bacterial growth which occurs in a nutrient medium containing varying quantities of salt. The organisms used were the staphylococcus pyogenes aureus and the bacillus coli

communis, and cultures were grown in a series of broth tubes containing from 0.5 to 12 per cent. sodium chloride. Quantitative estimations were made of the number of living bacteria added to the culture tubes and the number present after varying periods of incubation. With both micro-organisms proliferation occurred in 5 per cent. salt broth—i.e., in the strength of saline usually employed for surgical purposes; this was, however, much less rapid than in the lower salt dilutions. For example, in broth containing 5 per cent. saline staphylococcus pyogenes aureus increased after 24 hours incubation at 37° C. from 9 millions to 77 millions, and after three days to 708 millions. In broth containing 0.5 per cent. saline staphylococcus pyogenes aureus increased in 24 hours from 9 millions to 435 millions, and in three days to 1012 millions. In the 7 per cent. and 8 per cent. salt media multiplication was still further delayed. In the 10 per cent. and 12 per cent. salt cultures no proliferation occurred; the cultures of staphylococcus pyogenes aureus were still alive after 24 hours, but those of bacillus coli communis were sterile. It follows that when 5 per cent. hypertonic saline is applied to a wound the inhibition of growth due to the salt alone can only be very slight.

The majority of septic wounds heal rapidly if good drainage is provided and frequent dressings are applied. The choice of lotion seems immaterial provided the one selected is non-irritating and fresh infection is prevented. The ultimate recovery of the patient depends upon physiological processes, and if preference is given to any of the above reagents for routine treatment it would be to that which reinforces the physiological processes in the tissues of the wounds—viz., hypertonic saline solution.

In certain cases treatment with the so-called antiseptic lotions and hypertonic saline was not successful, and it was recognised that some improved method was required. The plan adopted was to select a few wounds which did not yield to ordinary treatment. These cases were made the object of a special investigation. Two antiseptic reagents were tried: (1) Eusol, as introduced by Professor Lorrain Smith and his collaborators¹; and (2) salicylic acid.

Treatment with eusol.—In eusol we possess a valuable and cheap antiseptic. In our experience the immediate effect of eusol is to sterilise the surface of the wound with which it comes in contact. Cultures taken directly after irrigation remain sterile. Numerous colonies, however, will develop on cultures taken after an overnight interval, and there is often no reduction of bacterial growth from day to day. The effect of the eusol is temporary only, because of the infection of the deep tissues. This is well recognised, and to meet the difficulty frequent application or continuous irrigation has been advised. In some cases, however, it is not easy to arrange for continuous irrigation, and whatever contrivance is adopted there is a tendency for the lotion to flow through certain channels to its exit, with the result that large areas of the wound do not get irrigated. In spite of these disadvantages, the clinical results obtained from eusol are very encouraging, and some cases have responded more rapidly to it than to other reagents. The following case illustrates its use:—

CASE 1.—Private, aged 19. A large abscess of the calf of the leg was opened; the pus grew staphylococcus pyogenes aureus. The cavity was irrigated with eusol and packed loosely with gauze soaked in eusol. Irrigation and the dressing were repeated twice daily, and each morning cultures were taken from the wound immediately before the irrigation. A series of cultures were thus obtained. From the first to the sixth day numerous colonies grew, and the cultures were indistinguishable from one another. On the seventh day there was a marked reduction in the number of colonies. On the eighth day only two or three colonies developed, and the subsequent healing of the wound was rapid. This series can be explained by the fact that free exudation from the abscess during the first six days diluted the eusol and washed it away from contact with the tissues. It was only when the exudation ceased that the antiseptic remained in contact sufficiently long for its action to be evident after an overnight interval.

In cases where eusol has not been a success the failure was apparently due to the fact that continuous treatment was impossible, and the effect of the antiseptic was transitory. Very little reagent is left in contact with the

¹ Brit. Med. Jour., July 24th, 1915; THE LANCET, Feb. 5th and 12th, 1916.