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ACUTE APPENDICITIS*

BY

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"Let us return to our ideal; early operation is the only safe practice."—J. B. Murphy, 1916.

Since I was invited to take part in this discussion I have often wondered what induced the officers of the Section to choose this admittedly important subject. It appears to me that everything that can be said on appendicitis has already been much better said over and over again. Perhaps we are apt to forget that while the message is the same the audience is constantly changing.

It was Murphy of Chicago, one of the greatest teachers of all time, who declared that every few years important subjects in surgery should be reviewed and discussed so that the lessons connected with their management could be constantly kept before the profession. I am assuming that in discussing this matter we are but fulfilling this very proper idea.

Some time ago I was startled by the remark made by the husband of a very ill patient on whom I had operated for appendicitis with a complicating peritonitis, and who, unfortunately, succumbed. The man afterwards said how terribly disappointed he was, considering that his wife was *only suffering from such a simple thing as appendicitis!* I suppose it really means that as the great majority of the patients recover, when the result is otherwise everyone is surprised and disappointed. But, this being so, it shows how great is the responsibility laid on our shoulders. Yet in my view the real reason which justifies the discussion is because as a profession we cannot but be impressed by the individual tragedies to which we are unfortunately witness, and because we must feel in our heart of hearts that many of them might have been prevented.

Mortality Statistics

After all, appendicitis is not inherently a serious disease, though its potentialities for evil are great and alarming. The Registrar-General has very kindly supplied me with figures which show that about 3,000 people die every year from appendicitis in the United Kingdom. This number represents 12 per cent. of all the deaths from gastro-intestinal disease and 0.61 per cent. of the total deaths registered. Some may think this is not as high as might be expected, but at the same time, since we must know that it is largely preventable, it is somewhat of a reproach to our profession. In order to endeavour to discover the mortality of the surgical treatment of this disease I have been furnished with statistics covering a period of five years from two of our great hospitals—the London Hospital and the Royal Victoria Infirmary, Newcastle-on-Tyne. The figures are as follows:

TABLE I.—*The Surgical Treatment of Appendicitis (Combined Figures for a Consecutive Five-year Period (1933–7) from the London Hospital and the Royal Victoria Infirmary, Newcastle-on-Tyne)*

	No.	Deaths
Acute cases (excluding localized abscess)	6,725	247 (3.67%)
Abscess cases	604	51 (8.44%)
Above two groups (all acute cases) ..	7,329	298 (4.07%)
All cases (acute, subacute, and interval) ..	9,933	308 (3.10%)

But I am not good at juggling with statistics, and I find that it is extremely difficult to get comparable figures from which one might draw perhaps some suggestive conclusions. I would, however, ask you to bear with me for a moment to consider some figures dealing with my own personal experience over the period of thirty-four years that I was in surgical practice in Newcastle-on-Tyne.

TABLE II.—*Appendicitis to End of 1934 (Newcastle-on-Tyne)*

	No. of Cases	Deaths
Group 1: Acute appendicitis without peritonitis ..	159	0
„ 2: Acute appendicitis with localized peritonitis	428	4 (0.93%)
„ 3: Acute appendicitis with flank or pelvic peritonitis, or both	230	22 (9.56%)
„ 4: Acute appendicitis with diffuse peritonitis ..	96	28 (29.2%)
„ 5: Appendicitis with residual abscess	64	5 (7.81%)
„ 6: Appendicitis with primary localized abscess	446	16 (3.59%)
„ 7: Appendicitis—interval removals	1,080	4 (0.37%)
„ 8: Appendicitis with primary complications ..	20	9 (45.00%)
„ 9: Appendicitis—no operation	0	—
„ 10: Appendicitis?—incidental removals ..	0	—
	2,523	88 (3.49%)

Groups 1 and 2 ..	587 cases ;	4 deaths	(0.68%)
Groups 1, 2, and 3 ..	817 ..	26 ..	(3.18%)
Groups 1 to 6 and 8			
(All acute cases) ..	1,443 ..	84 ..	(5.82%)
All Groups ..	2,523 ..	88 ..	(3.49%)

The Classification of Appendicitis

So far as I am able to judge there can be no classification of appendicitis that is not open to error and to which objections cannot be raised. I can only suggest that the simple grouping employed has proved most useful. May I just point out that it is in no way selective and that, as it includes all the cases, anyone may draw their own conclusions from the information provided.

It will be noticed that the basis of the classification is a pathological one, for the disease starting in the appendix spreads from this area as a radiating infection. In the

* Read in opening a discussion in the Section of Surgery at the Annual Meeting of the British Medical Association, Plymouth, 1938.

great majority of cases appendicitis at its inception is a local disease, but when the infection spreads a secondary nidus arises in the peritoneum and in some cases in the blood stream. Group 5 includes those cases in which a more or less diffuse inflammation, as in Group 4, has fortuitously localized, but with abscess formation which is not necessarily around the appendix; it may be pelvic or subdiaphragmatic or in the flank. In Group 6, on the other hand, the inflammation has gone on to suppuration, but around the site of the appendix, wherever that organ may happen to be situated.

Group 8 comprises those cases in which there were primary complications—that is to say, in which patients have come under treatment suffering from appendicitis but with some such complication as acute intestinal obstruction, pylephlebitis, advanced cardiac disease, pneumonia, or some other such condition. Group 9 was intended to include cases in which no operation was carried out, lest one might be accused of improving statistics by refusing to operate on bad risks. But the cases in which I have not operated have usually been those who refused surgical intervention, and these have been so few that years ago I ceased putting them in the table.

The heading “incidental removals” (Group 10) is included to give me the opportunity of saying that we ought not to count these cases in the statistics of appendicitis. If whenever the appendix is removed in the course of some other abdominal operation it is counted as an example of appendicitis, we can soon accumulate a very large series, but such a series can have no value so far as the problem of the treatment of appendicitis as an entity is concerned. The record goes back for many years, and includes those early days when I was formulating rules for my own guidance and learning technique. Many of those early operations were carried out in small industrial houses or country cottages.

If you will look at the figures you will see that the cases which reach the surgeon at an ideal stage—that is to say, while the inflammatory trouble is strictly limited to the appendix or in its immediate neighbourhood—can be operated upon with a mortality considerably less than 1 per cent. even in a reasonably large series like the 587 set out in Groups 1 and 2. But the extension of the infected process to the unprotected peritoneum, which brings the patients into Group 3, immediately introduces new factors which have a very serious bearing on the outlook. The involvement of the peritoneum in the pelvis, on the flank, or both, creates a new infective focus which may not readily subside as the result of removal of the appendix, with or without drainage. It is this group that furnishes a large proportion of the complications which provide such serious problems for treatment. These factors are reflected in the mortality, which in this group approaches 10 per cent. In these cases the infected fluid is free in the peritoneal cavity, and they might quite fairly be classed as examples of unlimited peritonitis, many of which are potentially general. But even accepting these considerations, if we add these cases to those in Groups 1 and 2 we get a series of 817, with a mortality of 3.18 per cent. The object of the classification, however, is to include all the cases so that we get a true picture of the mortality. If we do this and only exclude the cases operated upon in a quiescent interval we get a series of 1,443 cases, including that unhappy group where there are primary complications, with a mortality of not quite 6 per cent. But my chief point is that as a profession we must never be satisfied until we can manage to get

the great majority of cases treated by surgical means while they yet belong to Groups 1 and 2. If that could be done the experience of very many surgeons the world over shows that the mortality need not be more than 1 per cent. If this happy state can be brought about appendicitis might then be looked upon as the comparatively simple disease which it now is in the eyes of so many of the public. After all, the public look to us for guidance, and if it were universally insisted that very much better results would follow earlier intervention they would readily agree. To get the best results the co-operation of the public and of the profession is necessary.

In this matter of emergency surgery I do want to say what a great opportunity is presented in our large hospitals, or groups of hospitals like those under public authority control such as the L.C.C. or the Middlesex County Council. If agreement could be reached on a general classification which might be uniformly employed these hospitals could, in a few years, accumulate such a mass of statistics as would, let us hope, be useful in settling a good many problems which still remain unsolved. In this one respect we might take a lesson from Russia; I think it might be worth while. In their large emergency hospitals in Moscow they are trying out various methods of treatment checked by careful statistical records. It is a mass experiment which is extremely interesting, and may provide valuable guidance for the surgery of the immediate future.

Stage at which to Operate

In suggesting that the main consideration is the stage at which the operation is carried out, one can find a useful, though not entirely parallel, comparison in the treatment of ruptured peptic ulcer, for in that condition nothing makes so much difference as the time which elapses between perforation and the intervention. Here again may I just trouble you to look at some figures bearing on the matter and which speak for themselves.

TABLE III.—*Perforated Gastric and Duodenal Ulcers (Combined Figures of Mr. Grey Turner and Mr. Norman Hodgson to End of 1929)*

No. of Hours of Perforation in 6-Hour Periods	No. of Cases	Recoveries	Deaths
Up to 6	119	115	4 (3.36%)
7 to 12	148	129	19 (12.83%)
13 to 18	40	33	7 (17.5%)
19 to 24	21	15	6 (28.57%)
Over 24	37	18	19 (51.35%)
Total	365	310	55 (15.06%)

All cases operated upon within twelve hours : 267 with 23 deaths (8.61%).

Why is it that so often surgery is not invoked while the disease is still limited to the appendix? I do not believe that the delay is so much due to mistaken diagnosis as it is to the expectation that the patient will get well without operative intervention. We all know that many sufferers do get well spontaneously, but at the same time I think we must admit that once the appendix has given trouble it is likely to do so again, and that it may be the cause of other troubles and is much better removed. Nevertheless, with the knowledge that many cases get well, it is perfectly reasonable that some patients, and often for the most excellent reasons, should wish to take the chance. But how are we to know that improvement is really taking place—what simple rule will guide us?

One of my former colleagues, the late Mr. W. G. Richardson of Newcastle-on-Tyne, to whom I am much indebted for many valuable lessons in emergency surgery, used to teach that in appendicitis it is unwise to conclude that natural recovery is taking place unless *all* the symptoms are improving. I have long been convinced of the great wisdom of this rule, and if it were always observed many a life would be saved and many a long illness prevented. It is not enough that pain is diminishing if the pulse is going up, or that the pulse remains unaltered if pain is becoming diffuse or the temperature is rising. The progress of the case is only sure if all the symptoms are simultaneously improving.

Early Diagnosis

How are we to make the early diagnosis which will justify the prompt surgical intervention which is so important? Well, there are easy cases and difficult cases, and nobody is more ready to admit that I have often been confronted with problems in diagnosis which only an operation has solved. In the easy cases—and they are in the great majority—the cardinal symptoms, as set out by Murphy, will always be found, and they are so important that I make no apology for referring to them once again. These are pain in the abdomen, which may be sudden and severe but is rarely overwhelming; nausea or vomiting or some gastric disturbance with disinclination for food; general abdominal sensitiveness, sooner or later more marked over the right side; and elevation of temperature. Murphy insisted that the symptoms occurred in that order, and was accustomed to say, “When that order varies I always question the diagnosis.” But every case must be carefully considered, and I would say without hesitation that it is often indiscriminate diagnosis rather than hasty operation which brings early intervention into discredit.

The history of the onset is important; it may be sudden and severe, or more gradual. In the former case the patient may look very ill, and I have always attached importance to the testimony of those who know the patient and who can say that the aspect is altered. The rise in temperature may be slight, and Murphy used to point out that it may sometimes only be detected per rectum; but none the less I agree that it is never absent. It must surely be universally realized that the pain may be entirely epigastric or just around the umbilicus; but, wherever the pain, the tenderness is found only at the site of the appendix, and that is usually in the region of the right iliac fossa. In the presence of an acute appendicitis the pulse may be little affected; but as the condition develops it invariably quickens, and a steadily rising pulse is a valuable collateral sign. The condition of the tongue is seldom mentioned; yet it is invariably slightly altered even in the early stages, and, though difficult to describe, there is something about it that seems to me characteristic when associated with the abdominal sequence on which Murphy so much relied.

It was my friend Arthur Burgess who first impressed on me that it is not necessary to wait for rigidity before making the diagnosis. The mere difference in resistance as compared with some other part of the abdominal wall is enough to guide the experienced observer. This is especially valuable in the pelvic and retrocaecal cases, where the appendix is hidden away from the abdominal wall.

I would also emphasize that in appendicitis the tenderness is easily evoked by light palpation, and I am always gravely suspicious of the diagnosis in those cases in which it requires a deep and perhaps rather heavy palpation to elicit this sign. Murphy used to be very bitter about the

use of morphine in the treatment of suspected cases of appendicitis, and I well remember the cynical look on his face as he told his audience that patients so treated would recover in time to make excellent arrangements for their funeral! Rutherford Morison was equally emphatic, and used to tell us that if an abdominal pain was so severe as to require morphine for its relief then the case was one for operation. But in this matter my sympathies are entirely with the practitioner, for I know how insistent are the demands of the patient or the friends for relief. A single minimal dose of morphine may not mask the symptoms for too long, and as it wears off the return of pain is a certain sign of some grave condition, but the repeated small dose of morphine is fraught with great danger, and should never be employed when an abdominal emergency is in question.

It would go beyond the object I have in view to discuss the question of differential diagnosis, but there is one diagnosis that has certainly been responsible for many fatalities, and that is a diagnosis of abdominal influenza. I very much doubt if there is any such condition, and believe that it is usually only a handy explanation for some obscure inflammatory abdominal trouble, which in most instances has its origin in the appendix. From infancy to the age of 23 I myself suffered from numerous attacks which were confidently and repeatedly diagnosed as abdominal influenza but which were arrested for all time by the removal of a pathological appendix. But all cases have not so happy a sequel, and I could recount many tragedies due to this unfortunate diagnosis.

What can we do to help the young practitioner to recognize appendicitis at an early stage when operation is so insistent and so successful? Let us make more use of these common emergencies for teaching purposes. How often are we told on ward rounds that such and such a case is “only an appendix.” These emergencies should be demonstrated to our students in all their aspects whenever the opportunity arises, and they should see the operations, watch the after-progress, and keep records of what are now looked upon as such ordinary conditions as to be scarcely worthy of notice.

Treatment in Early Cases

The treatment of the cases in this comparatively early stage is very simple, for all that is necessary is to remove the appendix and when in doubt to put in a small rubber tube to act as a drain.

“The state is best governed as you cook little fish, without much busyness.”—Laotze.

It is perfectly true that there is often nothing to drain; but a small tube provides a track to the surface, and if the organisms do regain their activity after the removal of the offending organ such a track may mean an external discharge rather than an internal spread. At all events, I believe that a small tube properly placed often does good and never harm; but it should not be removed too soon, and I am accustomed to leave such tubes *in situ* for a week. If by that time there is no discharge they may safely be discarded. To the young surgeon I would most emphatically declare, when in doubt drain.

Complications of Peritonitis and Abscess

While, however, it is our plain duty as a profession to do everything possible to make an early diagnosis and to act upon it by prompt surgical intervention, one must admit that many patients are not seen until there are complications like peritonitis and abscess. Even in these circumstances I am convinced that they should be

regarded in terms of what relief may be provided by operation. But here I think we must be wise and recognize that some little delay may be an essential part of the management of the case and may be to the great advantage of the patient. For instance, in peritonitis where the abdomen is grossly distended, there is frequent vomiting, the pulse is quick, and there is obvious toxæmia it is essential to keep the case under observation for a few hours. During this time certain measures should be employed which may help the patient towards recovery by localization or so far improve matters that the necessary intervention may be carried out with more chance of success.

The stomach should be emptied by tube and the rectum by glycerin enema, while toxins are diluted by giving water by the bowel or intravenously. It usually greatly adds to the comfort of these patients, and I think may do some good, to apply heat to the abdomen, and during this period of preparation, the diagnosis having been made, a small dose of morphine may be extremely valuable. If, as sometimes happens, there is great improvement in the course of a few hours it may be wise to wait; but again the dictum of W. G. Richardson is to be the guide, and, unless all symptoms improve, then it is much wiser to make a small incision merely with the idea of giving exit to peritoneal exudate. In these circumstances a small incision or incisions under local anaesthesia, with the insertion of a tube, is all that is justified. The question of the removal of the appendix must be left to a later date. If, on the other hand, the patient arrives with clear indications of a localized abscess, convalescence will be aided and recovery helped by the evacuation of pus.

I have twice in my life seen patients with such an abscess die suddenly from rupture of the collection into the peritoneal cavity while waiting for absorption to occur, and many times I have seen the inflammation gradually spread and convert a local process into a diffuse peritonitis. In many cases of localized abscess it is possible to do a complete operation in the sense that the appendix is removed, but whether that is advisable or not must depend a good deal on the judgment, and especially the experience, of the operator. The life-saving measure is the evacuation of the pus, and for that a small incision with the insertion of a drainage tube is all that is necessary. The stage at which to re-intervene for removal of the appendix is a matter worthy of comment; but I do not want to go into that now, because it will sidetrack our discussion from its essentials. It is significant that in the large series of cases of appendicitis which I have quoted from London and from Newcastle-on-Tyne the localized abscesses (604) were attended with a mortality of something over 8 per cent. More difficult cases are that type in which the patient arrives with a very hard, localized, scarcely tender swelling in the iliac fossa. In such cases it usually means that the pus has already safely found its way into the bowel, which is a much more common event than its mere absorption, as I have repeatedly been able to demonstrate. If all is going well then, of course, it may be wiser to wait and to deal with the removal of the appendix as an interval operation; but again, unless all the symptoms are improving, I would have no hesitation in urging intervention.

The Late Stage

When can a case of appendicitis be said to be in a late stage? I have the greatest distrust of any rule in treatment which suggests that after a lapse of a certain

number of hours operation is inadvisable. I can never understand the rationale of such a dictum unless supported by an enormous mass of the most accurate statistical evidence. It rather suggests the Gilbertian situation that whereas at a quarter to twelve on one day the case ought to be operated upon, when that hour has struck it is already too late and the patient will have a better chance if treated by other means! Pathological processes do not attend on the clock, and whereas in one case diffusion of infection will have taken place within a few hours, in another this event may be delayed for days or may never occur.

Causes of Mortality

In endeavouring to evaluate the causes of the mortality I have been helped by my former assistant, Mr. A. Elliot-Smith, who has gone carefully into this matter in a considerable series of cases. His investigations tally with my own, to the effect that much of the mortality is due to complications. The main causes of death are undoubtedly an unarrested peritoneal infection, the formation of undetected abscesses in situations like the pelvis and the subdiaphragmatic areas, intestinal obstruction of various forms, cellulitis of the abdominal wall, and pulmonary infections. It is often suggested that the results of operations for appendicitis are largely influenced by the technique of the operator. This may have some bearing, but it is of very minor importance compared with the stage at which intervention is carried out. For instance, one operator, with certainly most excellent results, attributes a large part of his success to the fact that he never buries the stump of the appendix. I have always endeavoured to bury the stump, and I am equally satisfied that nothing but advantage has ever accrued to any of my patients from this step. I have lived too long in surgery to be influenced by the suggestion that any small detail of technique will alone make much difference in the mass results. All these things are of great interest, but I am equally certain that they are not essentials, and they must not be allowed to distract our attention from things that are.

I should be disloyal to my old school, however, if I did not once again urge the advantages of the oblique muscle-cutting incision of Rutherford Morison. For the early cases almost any type of incision will suffice, but for the later cases, and especially those presenting a lump, the oblique incision directly over the site of the mischief is much superior to any other. It has been a great satisfaction to me to find how readily my new associates at Hammersmith, who have all been trained in Southern schools, have appreciated the advantages of this approach. May I stress the importance of the careful closure of this incision in layers and with interrupted sutures of reliable stout catgut.

Treatment in Special Circumstances

There are certain circumstances in which acute appendicitis occurs which introduce special features that may have a bearing on its treatment. First of all in children, it is universally admitted that there are many pitfalls in diagnosis and that the disease may progress with alarming rapidity. To my mind this knowledge emphasizes the extreme importance of care in diagnosis in these little people. I want particularly to insist on the equal importance of following up a diagnosis of probable acute appendicitis by operation. Although we are all aware that diagnosis in children is difficult, in Newcastle-on-Tyne I was impressed by the great frequency with which

appendicitis was ultimately proved in cases in which our contributing doctors had sent the patients into the hospital with that diagnosis. In children the symptoms may vary rapidly, and many such cases appeared to have little the matter by the time they reached hospital, but when operated upon I nearly always found the appendix grossly and unmistakably diseased. Often the child will appear to be quite well and to have nothing but a little remaining tenderness over the appendix, and yet the appendix may be perforated and surrounded by pus.

In old people the peritoneum seems to lose its powers of natural resistance, and I am again satisfied that we should not postpone an operation because a patient probably suffering from appendicitis is aged. We should rather say that advancing age is a factor which prompts early operation. No one with any experience will overlook the fact that in the aged there are special difficulties in diagnosis: bowel growths, diverticulitis, and even prostatic mischief have not infrequently misled.

When appendicitis is a complication of pregnancy it demands early operation. The course of the pregnancy will seldom be interrupted by such intervention, and, in any event, whatever the risk so far as that is concerned, it is probably much less than the risk of a recrudescence of the disease nearer term, during labour, or immediately after. In my own experience I have only once had a patient abort, and I feel sure that was due to delayed intervention rather than to the actual intervention itself. The same applies to patients with heart disease, asthma, and pulmonary infections. In such cases local anaesthesia will often enable us to carry out life-saving operations with little anxiety.

I think we must admit that there may be a variation in the virulence of appendicitis, not only at different ages and in varying circumstances, but from time to time, depending perhaps on the seasonal variation in the organismal invasions of the gastro-intestinal tract. I was persuaded that in Northumberland there was some difference as between the country people leading a healthy open-air life and the town-dwellers, and I am quite prepared to hear that these differences are met with in other parts of the country. But these possibilities do not affect the general rule as to the necessity of prompt operative intervention.

The difficulty about all the plans which countenance delay in the surgical treatment of appendicitis is that they are apt to be abused, for the public and a certain section of the profession are only too ready to find an excuse for adopting any treatment other than operation. It is for this reason that I am afraid of any attempt at differentiation as between the cases which ought to be treated immediately by operation and those which may be left to a more convenient season.

Murphy used to deplore what he called "epidemics of so-called conservatism" in dealing with appendicitis, and I have myself often pointed out that the recurring advocacy of a waiting policy or delayed operation has almost invariably been followed by a wave of increased mortality.

Conclusion

Irrespective of interesting academic problems, I think it is essential that we should recognize that any acute condition of the appendix ought to be treated by operation without delay. I do hope that as the result of this discussion the message may once again go forth to the profession with no uncertain voice that appendicitis means operation, and that the earlier the operation the better the chance for the patient.

CARBOHYDRATE METABOLISM IN ANAESTHESIA: A REVIEW *

BY

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The production of surgical anaesthesia by the administration of ether or chloroform is accompanied by various metabolic changes, among which may be mentioned a rise of blood cholesterol (Reicher, 1908 ; Ducceschi, 1919 ; Mahler, 1926), a rise of blood fat (Bloor, 1914), increased blood phosphate (Marenzi and Gerschman, 1934), a diminution of blood potassium (Marenzi and Gerschman, 1932), interference with water metabolism, leading to dehydration of the bodies of nerve cells (Barbour, 1931), and disturbance of the acid-base ratio of the blood (Stehle and Bourne, 1924). More than all these, however, certain aspects of the alterations in carbohydrate metabolism have received attention from clinicians and from experimental investigators. Of such changes the most striking and the most widely discussed is the hyperglycaemia fairly constantly produced by some forms of anaesthesia.

Changes in the Blood Sugar

That the administration of ether produces in the dog both hyperglycaemia and glycosuria was shown by Seelig (1905, 1906). Macleod (1913) stated that anaesthesia induced but slight changes in the blood glucose, and two years later Macleod and Pearce (1915) reported that ether actually produces a fall in blood sugar during the first half hour of ether narcosis. Ross and McGuigan (1915), however, measured the hyperglycaemia produced by ether and chloroform and, later, Ross and Davis (1921) attempted to distinguish between the mechanism whereby blood sugar is raised by the two drugs. Since then it seems to have been universally accepted that ether causes hyperglycaemia. Some observers—for example, Mahler (1926), Mackay (1928), Mackay and Dyke (1928), Minnitt (1932), and Hospers (1933)—have recorded considerable increases in the blood sugar level, sometimes to more than 200 mg. per 100 c.cm.; others, such as Nakamura (1935) and Hasaura (1935), have not detected such large hyperglycaemic responses; whilst Pratt (1938) found that the effect of ether upon the blood sugar level may vary considerably from case to case, generally producing a moderate increase, sometimes not influencing it, and occasionally even producing a fall.

Much less information is available as to the hyperglycaemic potencies of the newer or less common anaesthetic agents. Acetylene (Fuss and Deura, 1932), ethylene (Hospers, 1933), and nitrous oxide (Minnitt, 1932 ; Hospers, 1933) all raise the blood sugar level, but not to the same extent as does ether. According to Prasad and Sen (1936) sodium evipan given intraperitoneally in the rabbit raises the blood sugar to a moderate degree, but the barbiturates, generally speaking (Heller and Nathan, 1933 ; Nakamura, 1935 ; Hasaura, 1935 ; Hrubetz and

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