glass applied to the skin. Similarly he describes in detail experiments in which he measures the amount of air consumed by a candle burning or by an animal breathing under a cupping glass immersed in water. When the candle goes out and the levels have been duly adjusted the water is found to occupy one-thirtieth of the space previously occupied by air; when the mouse dies, one-fourteenth. In neither case is it possible to kindle in the air that is left combustible matter by means of a burning-glass, as can readily be done in fresh air.

These experiments could not have been done in Harvey's lifetime because the conditions under which alone they could be carried out had not been defined by Boyle. Mayow carried them out with all precaution that could then be devised, and though they suffer from the defect that no account is taken of gaseous products of combustion or respiration, they open an entirely new chapter in the history of both chemistry and physiology. The alembic and crucible no longer constitute the entire armament of the chemist; there is something better for him to do than to go on for ever distilling off mercury from blood and urine.

"Clearly something in the air is absolutely necessary for life and enters the blood in respiration, for if the need for respiration were that the blood may be shaken up and divided into the minute particles by the movement of the lungs the animal should not die so soon, for the air that is left should be able to do this perfectly well; and as it is subject to nearly the whole pressure of the atmosphere there is no reason why it should not enter the expanded chest; for I have shown that it is the pressure of the atmosphere that causes it to do this. It is true the bluntness of our senses prevents us from seeing the passages by which the air enters the blood [just as it prevented Harvey from seeing those by which the blood passed from artery to veins]. They must be exceedingly short and minute, for they merely have to pass through the membranes of the lungs and they must be almost infinite in number. And yet in lungs that have been boiled and dissected an almost infinite number of perforations like the minutest points can be seen with the microscope. Whether they are the mouths of capillary trachea I cannot say.

"Animals and fire draw particles from the air so that it loses elastic force; that these particles are of the same kind in each case is established. If in a similar experiment to those previously described a lamp and a mouse are at the same time enclosed in a glass over water the lamp goes out first and the animal dies later. But the animal dies in about half the time that it would have been able to live had the lamp not been there. It is not suffocated by the smoke of the lamp, for the same result is obtained if spirit of wine is used; moreover I have tried to kindle with a burning glass, in a vessel in which an animal had died from exhaustion of the air, combustible material previously hung in it. I had protected a part of the inside of the vessel from the condensed breath of the animal by a piece of paper which I could pull away by a string passing out below the mouth of the vessel. But it would not take fire. I shall not however make a final statement on this because the season being winter and the sky almost continuously covered with cloud I was not able to repeat the experiment.

"When the lamp goes out or the animal dies the remaining space is filled with air diminished in volume but able to resist the pressure of the surrounding air. I have indeed ascertained that such air is possessed of no less elastic force than any other air, for when the pressure of the atmosphere is removed it expands with no less vigour than common air."

Mayow published nothing after the five tracts. Four years later he was elected to the Royal Society, on Hooke's nomination, left Oxford, and was married, and the following year died in an apothecary's shop off Covent Garden, and was buried in St. Paul's Church there. He was 39—the youngest of the Oxford quartette, and the first to die. The five tracts were translated into Dutch five years later, into German one hundred and twenty years later, in 1799, into French in 1840, and into English in 1807.

The only reference to his work for more than one hundred years after his death appears to have been made by Stephen Hales. His work was forgotten. His discoveries rediscovered were the starting point of modern chemistry. By that time men's minds had become ground in which the seed could germinate.

You will, I hope, think that in our commemoration it is fitting that he should be remembered in the twentieth century, if only because he was so sadly forgotten in the eighteenth.

ANAESTHESIA FOR OPERATIONS UPON THE GRAVID UTERUS.*

BY

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It is the intention of this paper to show how, by a wise selection of methods, the anaesthetist may collaborate with the obstetric surgeon to make his work more effective and the safety of the patient more secure.

Preliminary Considerations.—During pregnancy women tolerate anaesthetic drugs exceedingly well. Last year, at the Birmingham Maternity Hospital, nitrous oxide was administered to more than three hundred women for dental extractions at all stages of pregnancy, and there was not a single miscarriage. Ether, chloroform, gas-oxygen, and spinal anaesthetics are often administered for all kinds of surgical procedures, but, save in the presence of dangerous infections, such as peritonitis, it is rare for the pregnancy to be interfered with.

Operations on the uterus and its appendages, when in the gravid state, fall into three groups: (1) operations only on the uterus and its appendages; (2) operations on the uterine contents; and (3) operations on the gravid uterus together with its contents.

OPERATIONS ONLY ON THE UTERUS AND ITS APPENDAGES.

These operations are usually undertaken with the purpose of improving the course of the pregnancy, or of making normal and unobstructed labour possible; thus it may be necessary in the earlier months of pregnancy to replace a retroverted gravid uterus. Inasmuch as muscular relaxation of the abdominal wall is required, and cyanosis is not advisable, ether preceded by atropine is more satisfactory than gas or gas-oxygen.

Fibroid tumours (particularly those in the cervix) and simple ovarian cysts may obstruct the pelvic cavity; removal of these is often a matter of considerable operative difficulty. The aims of the anaesthetist are therefore abdominal relaxation, the avoidance of circulatory congestion and oozing from cyanosis, and the least possible disturbance of the kidney and liver functions. Perhaps the best compromise is obtained with chloroform, or a mixture of chloroform with ether. Gas-oxygen does not give sufficient relaxation, and the resulting tension and pressure on the uterus may produce an intrauterine haematoma, resulting in a miscarriage. Spinal analgesia is useful because it controls the bleeding.

Mr. Lewis Graham of Birmingham has permitted me to quote a series of six operations for myomectomy which were performed under a mixture of chloroform and ether without any untoward event. In one instance the fibroid was as large as a coco-nut and deeply embedded. After removal, the base of the placenta could be seen at the bottom of the wound in the uterine wall, but the pregnancy continued normally. By way of contrast, however, I may refer to a case, at the sixth month of gestation, in which an adherent degenerating fibroid was removed, under ether, with very great difficulty; the woman miscarried on the next day.

Accidents to ovarian tumours, such as rotation or infection, may render the patient acutely ill; in these cases the anaesthetist must help the surgeon to save the patient's life regardless of the pregnancy. Gas-oxygen is a very suitable agent, because anaesthetic toxæmia and post-operative collapse are reduced to the minimum. Indeed, relaxation in these conditions is obtained with comparative ease. Ruptured ectopic gestation is usually best dealt with under gas and oxygen. But in a case of ruptured tubal gestation, which was complicated by severe bronchopneumonia, a spinal anaesthetic was employed with a satisfactory result.

*A paper read in opening a discussion in the Section of Anaesthesia at the Annual Meeting of the British Medical Association, Winnipeg, 1930.

OPERATIONS ON THE UTERINE CONTENTS.

Here, although in the course of the operation the uterus may be incised or manipulated, the surgeon endeavours to effect his purpose on the contents of the uterus without producing any permanent injury or alteration in the condition of the uterus and the tubes. Taking this group on a wide scale, we have to consider anaesthesia for (1) manipulation of the foetus to obtain good position and satisfactory presentation before labour; (2) normal labour and labour complicated by protraction, manipulation, instrumentation, and so forth; (3) emptying of the uterus by direct operation, including evacuation of the premature foetus or mole, and Caesarean section for the viable foetus.

Manipulation of the Foetus in utero.

A general anaesthetic is not usually required, for the necessary manipulations are quite endurable, and the expectant mother is not over-sensitive; but in exceptional cases the malplacement may be intractable or the patient may be over-anxious. Complete muscular relaxation under ether may help the difficult manipulation, while if the psychological factor is the only difficulty, light gas-oxygen anaesthesia is valuable. Spinal analgesia will relax the abdominal wall completely, but the uterus in such circumstances is firmly contracted, and thus it may not be possible to turn the foetus.

Labour.

Early in the history of anaesthesia the pain of normal labour was treated by inhalations of ether and of chloroform. Sir J. Y. Simpson, in Edinburgh, was the first to demonstrate the anaesthetic properties of chloroform, and his vigorous advocacy of its use in midwifery was soon supported by the consent of Queen Victoria to be herself chloroformed in childbirth—thus chloroform *à la reine*!

Mrs. Stanley Baldwin has recently led a campaign to provide "anaesthetics for British mothers." I think that medical opinion is agreed that the matter as raised by Mrs. Baldwin is debatable on several grounds.

Although millions of mothers have received chloroform, a few points in its use may be worthy of mention. During the first stage chloroform is rarely needed. In the second stage amnesia should be aimed at. Analgesia and sometimes light anaesthesia are permissible, but full anaesthesia stops the uterine peristalsis, and post-partum haemorrhage becomes a serious risk.

Many times it has been said that chloroform is safe for pregnant women, but that is not quite true. Light chloroform *à la reine* is indeed surprisingly safe, but I know two medical practitioners each of whom has lost a patient from heart failure during the application of forceps under full chloroform anaesthesia. Removal of the mask should precede application of the forceps. To allow the patient to administer chloroform to herself by squeezing the bellows of a Junker's inhaler is an accepted practice, but it is necessary to be careful that the Junker's bottle is tested and fixed firmly out of harm's way, lest a pool of chloroform in the bed lead to severe burns.

Ether was used for midwifery before chloroform was discovered. It is pungent for the patient; it causes secretion, bubbling, and cyanosis when atropine has been withheld, and the stages of amnesia and analgesia are not maintained quite so readily as with chloroform. Nevertheless, W. J. McCardie, after long experience, maintains that ether may prove a most valuable stimulating analgesic for a patient who is exhausted from a long labour.

During recent years gas-oxygen has received much attention in connexion with midwifery. H. E. G. Boyle, a pioneer in this respect, recommends that a gas-bag, distended with a four-to-one gas-oxygen mixture, should be held in the patient's hand. Following instructions which have been given to her, she takes four or five deep breaths from the bag when she feels a pain coming, and strains down. Thus partial loss of pain, good pressure from the abdominal wall, and strong uterine contractions are secured. Dr. Boyle thinks that oxygen itself promotes contraction, perhaps by eliminating sarco-lactic acid and thus preventing muscular fatigue. A little ether may be added when the head is passing over the perineum, and

the child is then born in a lively condition. The method is of undoubted value, but the cumbersome nature of the apparatus tends to limit its employment to maternity hospitals and clinics. In the more protracted and serious complications of obstetric work, such as high forceps manipulation, craniotomy, and the like, gas and oxygen, by its low toxicity and freedom from after-effects, has saved many lives.

The new anaesthetic drug avertin has been tried in this connexion, and Dr. Doris Wall reports as follows:

"Avertin is pleasant in its induction, and has no action upon the foetus. There are no unpleasant after-effects, and there is the advantage of complete amnesia, extending some hours after the delivery, and long after the analgesic effect has passed off. The depth of anaesthesia produced is about that of twilight sleep, and when given in divided doses to a primipara, it can be made to last throughout the second stage, although this is sometimes difficult. Its duration appears to be increased by injecting the drug dissolved in milk.

The rate of the pains is slowed down to about half, although their intensity is only slightly diminished. If any manipulation is required, avertin must be supplemented with a little ether or with gas and oxygen."

I find that colonic-oil-ether has a similar effect, but during induction it is not so pleasant for the patient; it leads to more congestion and to deeper anaesthesia.

Spinal analgesia has been employed by many workers, and Dr. Cosgrove in 1928 reported unequal results; the uterus was often flaccid and the perineum was relaxed, probably due to a low injection—a caudal block. High intrathecal injection, with muscular paresis and analgesia up to the costal margin, always produces relaxation of the trunk and lower limbs, including the abdominal wall and the perineum. At the same time, in my experience, the uterus contracts tonically.

The effects of this contraction, I find, differ according to the stage of labour at the time of the injection. Injection of a spinal anaesthetic before the os is fully dilated leads to stopping of uterine propulsion, and the foetus does not progress until the anaesthetic effect has worn off. Injection after the os has dilated to the full extent may enable the accoucheur to compress the uterus sufficiently to expel the child with comparative ease, or forceps may be applied, or finally the foetus may not progress at all. Injection after the head has descended through the pelvic canal may lead to immediate delivery, especially if the child is small; usually the child is readily expressed by gentle manual pressure on the abdomen.

It will be seen that the indications for spinal analgesia in normal labour are not impressive, but in a small series of cases, in the presence of severe heart disease, I have found it useful. I inject the solution at the beginning of the second stage, when the os is fully dilated and the expulsive pains are strong. It is at this time that the diseased heart commences to run the gauntlet of overstrain. The immediate relief from straining down helps the patient to a remarkable extent. Forceps can usually be applied with comparative ease, and slow steady traction, associated with pressure on the uterine fundus, yields a satisfactory delivery. Birth of the placenta follows usually at once, for the organ is exfoliated by the strong shrinkage of the uterine wall. Post-partum haemorrhage has not occurred in my experience, and indeed bleeding has been scanty. Epidural anaesthesia has received some attention, but Dr. Rucker in 1928 reported that he found failure to produce analgesia to be not uncommon, and that is a serious drawback.

We conclude therefore that, in labour, chloroform is the most generally useful anaesthetic, while gas-oxygen is the most safe. Analgesia, by either the spinal or the local technique, has but a limited field. I may add that a woman told me recently that in 1918, when she was near term, an air raid frightened her so much that she was unconscious for two days, during which time her baby was born.

Emptying of the Uterus by Direct Operation.

Evacuation of an immature foetus, a mole, or other retained products of gestation may require a simple dilatation and curetting, or division of the cervix may be

advisable. Dilatation under chloroform is attended with the risk of reflex cardiac syncope; gas-oxygen often fails to relax the legs sufficiently to allow of a satisfactory lithotomy position, and with all forms of general anaesthesia the risk of dangerous post-partum haemorrhage is very grave. Considerable loss of blood is not uncommon, while fatal haemorrhage has occurred in the practice of many experienced gynaecologists.

At the Birmingham General Hospital, Professor Beckwith Whitehouse, Mr. Alfred Danby, and the anaesthetists have come to regard spinal analgesia as a valuable safeguard against this danger. With analgesia up to the level of the umbilicus, we find that strong tonic contraction of the uterus is the invariable rule. The loss of blood at the time of the operation is remarkably small, the post-operative loss is lessened, and the firmly contracted uterine wall offers satisfactory resistance, so that the curette or the ovum forceps can be employed without much fear of perforation of the uterus. The presence of phthisis is often an indication for evacuation of the uterus, and because inhalational anaesthesia is undesirable, spinal analgesia has proved most helpful in a considerable series of these cases. The toxæmias of pregnancy, diabetes mellitus, kidney disease, and heart disease are complications which are rendered less dangerous by the use of spinal analgesia for this operation.

Anaesthesia for Caesarean Section.

Inhalational anaesthesia is the usual method employed in Caesarean section; chloroform, ether, nitrous oxide-oxygen, ethylene-oxygen, and acetylene-oxygen have their advocates. The aims of the anaesthetist are to avoid poisoning the mother with the drug, to prevent cyanosis, to keep the circulation brisk and the uterus free from congestive engorgement, and to allow the baby to be born in a lively condition, with the least possible amount of the anaesthetic drug in its circulation, so that it may cry and expand its lungs at once.

It appears, therefore, that the gases nitrous oxide and ethylene are the more satisfactory anaesthetics because they are not toxic and because they are rapidly eliminated from the baby's blood stream.

In any case we advise that morphine should be withheld before Caesarean section, and that the anaesthetic should not be commenced until everything is in readiness for the operation; that is to say, the skin should be prepared, the towels adjusted, and the surgeon have put on his gown and gloves. The heavy abdominal contents may press on the heart and the bases of the lungs, so that additional oxygen may be necessary until the uterus has been emptied. After the extraction of the child, anaesthesia may be deepened by the addition of a little ether. Considerable experience with general anaesthesia for Caesarean section has shown that a smart haemorrhage from the incised uterine wall is the rule, and, not infrequently, it may be some minutes before the injection of pituitrin and ergot, together with the application of hot towels and massage of the flabby uterus, induces the organ to contract down and to arrest the bleeding.

In December, 1922, Professor Beckwith Whitehouse and I employed spinal analgesia for Caesarean section in a woman, aged 29, who was suffering from diabetes mellitus. We reported the case, together with a second, at a meeting of the Section of Obstetrics and Gynaecology of the Royal Society of Medicine in 1923, and we laid special emphasis on certain advantages which spinal analgesia presented. Powerful and sustained tonic contraction of the uterine wall rendered the uterine incision almost bloodless, and the suture line was tight and accurate. The child cried immediately after extraction, and the mother made excellent progress. Since that time I have employed spinal analgesia for most cases of Caesarean section in which the patient and the surgeon were willing.

The account of the technique and of the results, which I shall now give, is illustrated by the analysis of one hundred cases of which satisfactory records have been available. The patients were treated at the Birmingham General Hospital and Maternity Hospital, and in private practice. The majority of the cases were operated upon by Professor Whitehouse, to whose interest and initiative

this work owes a great debt. Sedative drugs, such as morphine, were not given until after the delivery of the child, in order that the child might be born free from respiratory depression.

It might be thought that these women would be panic-stricken at the idea of such an extensive procedure taking place while they were conscious. But even the most apprehensive of women, once the injection has been accomplished, settle down quietly with the will to go through with the business. In eighty replies to our inquiry as to their progress in hospital and subsequently there has not been a single complaint concerning the method. One woman who had undergone Caesarean section on two occasions, the first under spinal and the second under general anaesthesia, called upon me the other day to express her gratitude and her preference for the spinal method. In four instances patients in this series asked for spinal analgesia for a second Caesarean section, although one of them had suffered from a severe post-anaesthetic headache on the first occasion.

So much has been said and written on the different methods of producing spinal analgesia, such as light and heavy stavaine, spinocain, novocain, percaine, and tropacocaine, that I shall not dwell at length on the subject of technique. In this series 1 c.cm. of a 10 per cent. solution of novocain was used on one occasion with success, but for the remaining ninety-nine the anaesthetic solution employed consisted of a 5 per cent. solution of tropacocaine in normal saline. This solution has a specific gravity of 1.016, and it is therefore heavier than cerebro-spinal fluid, whose specific gravity is 1.006.

According to the size of the vertebral canal 1.75 to 2.25 c.cm. of this solution is injected into the second lumbar space, while the patient lies on her left side. We have formed the opinion that it is wise to prevent excessive loss of cerebro-spinal fluid. In a test series some years ago headache occurred in nine out of thirteen patients where more than 5 c.cm. of fluid escaped. The patient is turned gently on to her back; her eyes and ears are covered, but her face is left free, lest she complain of feeling stuffy. The table is tilted 25 degrees from the horizontal, with the head lowest. Analgesia develops to the level of the costal margin, or even as far as the level of the nipples. Failure to produce analgesia up to this level occurred only in two cases, due probably to an insufficient bulk of the solution.

Special technique is but rarely necessary for the actual lumbar puncture. In seven cases gas-oxygen was given throughout the operation, but, although the uterine contraction was satisfactory, the child was dazed for a few minutes after birth. A single dose of ethyl chloride provides one minute's anaesthesia, during which the back muscles are relaxed, the lumbar injection is made, and apprehensive individuals, after regaining consciousness, soon settle down. Dryness of the mouth is the source of much discomfort, but satisfaction is derived from the sucking of the end of a wet pad of gauze.

As soon as the skin becomes anaesthetic, we notice that the uterus appears to bulge more prominently, and it becomes more hard to the touch. When exposed, it is found to be firm and wrinkled with vertical ridges. The direction of the ridges suggests overaction of the circular muscle fibres, and Whitehouse and I have adduced evidence experimentally to show that spinal analgesia produces strong contraction of the circular fibres of the uterine muscle. This gripping effect of the uterus explains the failure of spinal analgesia, when given for miscarriage or labour, to expel the uterine contents.

In about half the cases the pressure exerted by the firm erect uterus on the abdominal contents caused retching, but in nearly every instance the discomfort and the retching ceased as soon as the child had been extracted and the uterus had contracted down. Notwithstanding the necessity in some individuals of opening into the uterine cavity through the placental site, when anterior, severe bleeding did not occur in a single instance. Pituitrin and ergot were reserved for the relaxation of the uterus, which sometimes happened after the effect of the tropacocaine had passed off. The ischaemic pallor of the uterine wall was always remarkable; indeed, in the majority of cases,

the total loss of blood during the entire operation did not exceed one tablespoonful. Fifteen patients were in labour at the time of the operation, and eighty-five were not in labour; the uterine contraction was equally successful in all of them.

Provided that narcotic drugs have been withheld, the child kicks and cries immediately it is withdrawn from the uterus. For a tired foetus, at the end of a long obstructed labour, in many instances this freedom from drugging at Caesarean section spelt life instead of death. The placenta is extruded by the strong contraction of the uterus, and the membranes rarely present any difficulty. Suture of the uterine wound is performed neatly and firmly, for the edges are clean-cut, and any tendency to relax subsequently actually increases the tension of the sutures.

After completion of the operation, the patient is carried to bed very gently, and her legs are elevated higher than the head. The lower half of the mattress is raised so that the legs are kept up, with the body horizontal and the head on a pillow. This position is maintained for five or six hours, and for twenty-four hours every effort is made to keep the patient quiet. A few hours after operation the uterine pains may be severe, and morphine is a great help. At one time we employed scopolamine in addition, but an anxious case of violent mania dissuaded us from the use of this drug. Abdominal distension for two or three days occurred in 20 per cent., but this is a frequent sequel to any abdominal section. During the periods of influenzal epidemics, and in sufferers from bronchitis, mild lung complications occurred, but there were no fatal cases from pneumonia.

By far the most unsatisfactory aspect of this procedure was "spinal headache," which occurred in 24 per cent. of this series. The headache started within twenty-four hours of the operation; it was suboccipital in location, and lasted, either continuously or intermittently, for one hour or for as long as a fortnight—in the majority of cases for twenty-four hours. Undoubtedly headache occurs after plain diagnostic lumbar puncture, after spinocain, novocain, stovaine, and percarine. There is good evidence that the following precautions are valuable: (1) use only solutions which have been freshly prepared; (2) do not allow much cerebro-spinal fluid to escape; (3) avoid puncturing the blood vessels on the anterior wall of the vertebral canal; (4) do not inject air bubbles; and (5) handle the patient gently; do not move her more than is necessary, and keep her quiet for twenty-four hours after operation.

There were no permanent complications attributable to spinal anaesthesia; the method was especially valuable in cases of phthisis, heart disease, kidney disease, diabetes, and goitre causing tracheal obstruction. Only one patient died at, or just after, operation, and she was actually expiring from heart failure before the operation commenced.

I have gone into this method at some length, for Professor Whitehouse and I believe that it is valuable, if carefully carried out.

OPERATIONS ON THE GRAVID UTERUS AND ITS CONTENTS.

Hysterectomy of the gravid uterus in the later stages of pregnancy is a severe procedure. Most frequently the operation is called for in the presence of concealed accidental haemorrhage, or for severe sepsis in the pelvic organs. It is one of the most anxious operations of surgery.

The patient is toxic, suffering from shock, and bloodless. The more powerful anaesthetic agents, chloroform and ether, disturb the patient too much; their use is followed by serious post-operative reaction, and pneumonia or failure of the heart or kidneys may follow.

Spinal analgesia may produce a dangerous fall in blood pressure in a patient who is already nearly pulseless. But one patient, aged 26, after Caesarean hysterectomy under "spinal analgesia" in 1923, although she suffered from extremely severe post-operative pneumonia, recovered and reported this year that she was in good health.

Gas-oxygen is a most valuable aid. Eight Caesarean hysterectomies were performed under gas and oxygen for concealed accidental haemorrhage; each patient was nearly

in a dying condition when the operation was commenced. One patient died half an hour after the operation was completed; one died on the sixteenth day, but the remaining six recovered.

In conclusion, therefore, I would summarize my views as follows.

1. By a wise choice of method, the anaesthetist may be able to offer valuable help to the obstetrician and to the gynaecologist.
2. In the more severe procedures, gas-oxygen is the best agent for general anaesthesia.
3. Spinal analgesia has an important place in the technique of Caesarean section.

I have to offer my thanks to Mr. J. T. Hewetson, Professor Whitehouse, Mr. Lewis Graham, Miss Hilda Shufflebotham, Mr. Alfred Danby, Mr. Kenneth McMillan, and Mr. R. P. Graham for permission to refer to patients who have been under their care. To Sister M. H. King of the General Hospital, and to Sister Knight of the Maternity Hospital, Birmingham, I owe my grateful thanks for very ready help.

THE DIAGNOSIS OF UNDULANT FEVER.*

BY

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It is becoming increasingly apparent that infection with organisms of the *Brucella* group, particularly with the bovine type of *Br. abortus*, is by no means always followed by typical undulant fever. Persistent malaise, often accompanied by irregular fever, chronic ill-health, obstinate headache, joint pains, neurosis, certain skin rashes, abortion in women, and focal infections of the internal genital organs in men, seem to be not uncommon manifestations of *abortus* infection. Any attempt, therefore, to ascertain the true frequency of disease caused by this organism must take into account not only the clinically recognizable cases of undulant fever, but also those numerous cases of illness in which no definite diagnosis has been made.

The methods available for the diagnosis of *Brucella* infections will be dealt with in turn.

THE AGGLUTINATION TEST.

This is best performed by mixing graded quantities of the patient's serum with a formalized, heat-killed suspension of *Br. abortus*, incubating in a water bath at 55° C., and reading the results after four and eighteen hours. A strain of *abortus* should be selected that has been recently isolated; many strains after continued subculture in the laboratory tend to lose their agglutinability. Enough agglutinating suspension may be prepared at one time to last for several months. There is no necessity, in England at least, to use more than one strain; *Br. melitensis* and the bovine and porcine types of *abortus* are agglutinated to a more or less equal degree by a serum prepared against any one of them, and the idea that it is possible to distinguish between these three types by direct agglutination is erroneous. In Tunis, however, according to Burnet¹ two distinct antigenic types of *melitensis* are met with, necessitating the use of two suspensions in routine agglutination tests.

The serum should be diluted from 1 in 10 to 1 in 5,120; if only one or two dilutions are put up, a certain number of significant reactions will be missed.

The interpretation of a positive agglutination reaction is often a matter of considerable difficulty, and demands close co-operation between the clinician and the bacteriologist. Many workers have emphasized the dangers of non-specific agglutination. It is noteworthy that this phenomenon has been met with chiefly in areas in which undulant fever is endemic. Evidence has been accumulating to suggest that in such areas a certain proportion of the population is suffering from a latent *Brucella* infection, and that the occurrence of agglutinins in the serum of these persons is really the result of infection, and

* Paper read in the Section of Bacteriology, Pathology, Physiology, and Biochemistry at the Annual Meeting of the British Medical Association, Winnipeg, 1930.