An Address

ON

THE PREVENTION AND TREATMENT
OF PUERPERAL INFECTIONS.

BY

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No subject of so much importance to the happiness and equanimity of the general practitioner and to the well-being of the lying-in woman as the prevention and treatment of puerperal infections can ever pall or become commonplace so long as progress is delayed.

Of late various attempts have been made to focus attention on this point and that; but I venture to think that, as in all other debatable questions, the multitude of "essential points" indicates the uncertainty of our outlook and the doubtful value of some of our methods.

I have nothing new or striking to bring before you to-day; I shall endeavour, however, to look at the matter broadly and practically, and attempt to indicate in what way further progress may be made at the present time.

PROPHYLAXIS.

One of the most disturbing features of the mortality rate in regard to puerperal sepsis is the fact that the maternal mortality from infective conditions, which to-day should be almost negligible, is not decreasing as we have a right to expect. Indeed, in the Registrar-General's last annual report the mortality is shown to be greater than in any previous year for fourteen years. It is probable, moreover, that if we could exclude the epidemics that used to occur in maternity hospitals and in the practice of certain midwives, and which we now know were the result of easily preventable contagion, the present mortality rate would be found to be not greatly different from that obtaining in pre-antiseptic days. In other words, while epidemics have been banished the isolated case still runs an undue risk from causes that are preventable. Another important matter brought to light by recent statistics is that cases attended by doctors more often suffer with puerperal sepsis than those attended by nurses alone.

Is it possible in any way to account for this deplorable state of affairs? I think so, and in a few words. Cases in which there is no manual or instrumental interference are comparatively immune to puerperal sepsis—not completely of course, as I shall explain later, but almost so.

The importance of this is at once evident in regard to the cases attended by midwives. In all difficult labours a doctor is summoned to deal with the case. In such circumstances interference may often be necessary. This is a class of case with which I shall deal separately, because it must clearly be understood that even in such circumstances sepsis should not follow the operations performed.

Unnecessary Interference.

Before considering the general question of the prevention of sepsis when interference is necessary, I must say a word—and I think the time has come when someone should speak plainly—about unnecessary interference. In doing so I make all allowances for the fact that women of the present day, with their excessive indulgence in athletics and mental excitements, are laying up a store of difficulty for themselves should they be fortunate enough to bring forth child, and for the adverse conditions that exist amongst women workers in large industrial centres. We all know the athletic young woman with her resistant pelvic floor, and the woman "living on her nerves" who will not willingly or cannot tolerate a normal, let alone a tedious, inert labour. We are well acquainted with the stunted growth and small pelvis of many women in factory districts. But allowing, I say, for all these embarrassments, which are the penalties of modern life, there is still a large number of cases in which interference is practised without scientific indication.

Twenty-five years ago "meddlesome midwifery," as it is called, was much less common than it is to-day, in spite of the fact that most of the procedures now practised by the

* Delivered before the North Staffordshire Medical Society on April 21st, 1921.

general practitioner, such as internal version and forceps delivery, were then in vogue. The student was taught in those days, as I hope he is to-day, that such operations are only to be practised in cases of real necessity, and that the necessity must be the mother's or the child's, and not that of other patients or of other calls.

Most practitioners of to-day, in contradistinction to those of the past, are surprisingly expert with the forceps; but I do not think the good done with these instruments adequately atones for the damage that too often follows the indiscriminate use of them. Familiarity is apt to breed contempt in all of us, and we are apt to find a too frequent use for that with which we are proficient. I realize, however, that in an appreciable number of cases the forceps are employed from what I may call humanitarian motives—to save the mother pain or to appease an anxious husband. That is moral cowardice to which we are all prone. But there are, I am afraid, many who make a practice of terminating with forceps nearly every labour at which they are present—more often than not with forceps taken from a "midwifery bag" which is far from clean and very imperfectly sterilized.

If the maternal mortality and morbidity rate is to be diminished, to say nothing of the number of operations for prolapse and other lesions due to hurried parturition, this practice must stop. It must be held to be a discreditable thing to terminate labour with forceps to placate the patient or to save the time of the practitioner, however skilful he may be.

Again, it should be a point of honour with all those who practise midwifery that no parturient woman shall be examined unless the examiner wear a sterilized glove. Even then the examination is best conducted per rectum, as Eardley Holland has suggested.

While I am convinced that unnecessary interference—accompanied, of course, by imperfect asepsis—is largely to blame for the present mortality rate in regard to puerperal infections, I do not wish for a moment to infer that there are not other considerations of great importance. It is, for instance, necessary for the practitioner to be fully acquainted with all the circumstances favouring infection in the parturient woman if he is successfully and safely to accomplish obstetrical operations in cases of necessity; and in this matter sound judgement as to the correct procedure may be a deciding factor in the result.

Natural Defences against Infection.

Normally there are two natural defensive arrangements for the safety of the mother. Towards the end of pregnancy there is a moderate leucocytosis in the circulating blood, and the vagina maintains its acid—lactic acid—secretion. But in circumstances not yet fully understood there may be a little or no increase in the number of leucocytes in the blood, and the acidity of the vagina may be considerably reduced or completely neutralized. The leucocytosis is a second line of defence, while the normal acid secretion of the vagina is the first. It goes without saying that the resistance of a healthy young woman is much greater than one weakened by malnutrition or disease.

The Points of Entry.

After normal parturition there is a large raw surface, the placental site. This is favourably placed for aseptic healing if no organism be present; but in the presence of infection it is most unfavourably situated in a cavity with only a potential outlet, and every blood clot closing a venous sinus is for bacteria an excellent nidus at body temperature.

While the placental site is nearly always the place of entry of the organisms in the more serious generalized puerperal infections, any laceration of the cervix, vagina, or perineum may form a point of entrance. It behoves us, therefore, to ensure healing by first intention in all lacerations, however caused. Neglect of this precaution often leads to the wound becoming septic; if the obstetrical operations have not been aseptically conducted or the environment of the patient be bad. It is interesting to note how well a sutured wound in a vascular area will heal, even in the presence of bacteria. An attempt is usually made by the practitioner to repair a lacerated perineum, and a certain amount of healing generally takes place, although the ultimate anatomical result is not always good. I always teach my students to insert sutures

accurately before laceration of the perineum occurs, if this appear to be inevitable. Accounts of how this should be done have been published, so I shall not discuss the procedure further. The cervix and vagina, however, usually escape attention at the time of labour, probably owing to the greater difficulty of discovering lesions in these situations.

Types of Infection.

We have heard a good deal lately about the question of autoinfection, by which means the patient becomes infected, either at the placental site or in some laceration produced in the birth-canal, with bacteria present at the time of delivery.

Pneumococcal infection, although rare, is not unknown. I have seen infection with this organism of the placental site, with death of the patient, follow an apparently normal labour during which not even a vaginal examination had been made by the doctor or the nurse in charge. Likewise, the gonococcus, which is too frequently present in the genital passages, and is more or less indifferent to the acid secretion of the vagina, may cause infective lesions; but, as a rule, gonorrhoeal infections remain localized.

With regard to streptococcal autoinfection there has been much controversy. It is now generally agreed that even in those cases in which streptococci have been isolated from the vaginal secretions prior to parturition, puerperal infection has by no means necessarily occurred. The presence or absence of these organisms has been shown to be closely related to the cleanliness of the patient; and it is probable that sexual intercourse at the end of pregnancy accounts in many cases for the presence of streptococci in the vagina. This is a practice against which it is our duty always to warn our patients; yet how rarely offered is the advice!

With these exceptions, and conceivably with such remote possibilities as infections by *Bacillus typhosus* and *Bacillus diphtheriae*, it is wise to regard autoinfection with suspicion. I believe, as I have already indicated, that death from puerperal infection is extremely rare after a normal labour in which there has been neither vaginal examination nor operative interference. In a vast proportion of all cases the bacteria are carried to the site of infection by the accoucheur or the nurse. It is therefore neither right nor courageous for the obstetrician to shelter under the possibility of autoinfection and lack of resistance on the part of the patient until such conditions have been proved beyond doubt by the scientific means at our disposal. Moreover, it must be remembered that these matters can be investigated before labour commences.

The most serious effects are produced by the streptococcus, which, according to my own experience in many cases investigated, is practically always present in generalized infections, even though other organisms be also found. *Bacillus coli communis*, *Staphylococcus aureus*, and *Bacillus aerogenes capsulatus* may occur, the first mentioned with considerable frequency. All these organisms are constant denizens of the bowel and the vulva.

Bonney, as many of you will know, thinks that the situation of the anus is a serious blemish in the foresight of—Evolution, shall I say? I do not agree with him; I think it is a danger spot, but it is so evident that it becomes a danger signal. The skin surface of the vulva is no less dangerous; indeed, a piece of unpurified vulval skin and hair placed in the uterus would probably be far more deadly than a spoonful of faeces. Moreover, faeces look infective, whereas the vulva does not, and the latter, therefore, constitutes a danger too often unsuspected—a danger so great that many of the investigations of skilled bacteriologists concerning the flora of the vagina have been vitiated. I fancy that Evolution has made us fairly resistant to the organisms of the rectum by virtue of our cloacal ancestors. I have never seen it suggested that the gradual disappearance of *Ornithorhynchus* is due to post-ovoviviparturitional infection. Further—and this is important—I do not think serious puerperal infection forms a regular part of the history of cases in the human subject in which there has been complete laceration of the perineum into the rectum. Such an injury is no more prone to serious infection than is that in which the laceration is partial.

However that may be, it is quite certain that infections with the organisms of the bowel do occur; nevertheless I do not think we should blame Evolution, which has

made no secret of the matter, but rather the careless attendant who contaminates his hands, in spite of the danger being obvious.

With such perils awaiting the incautious, is it any wonder that the chief element of safety is a negative one—non-interference? By non-interference the two chief factors leading to puerperal infection may almost certainly be avoided: organisms are not carried into the birth-canal, and lacerations, especially of the vagina and cervix, through which bacteria may gain entry, are less liable to occur.

Asepsis in Obstetrical Operations.

When interference becomes necessary, a surgical operation is performed, as Victor Bonney has so wisely emphasized. Every practitioner should, therefore, carefully foster in himself what I may call conscientiousness in regard to asepsis. No makeshift must satisfy him. While normal labour is physiological and there is no justification for interference, abnormal labour, on the other hand, is so serious—the possibilities of infection are so great—that nothing must be left to chance.

In the first place, every care must be taken to preserve the acid secretion of the vagina; consequently preliminary douches should never be employed. In the second place, every possible precaution must be taken by the practitioner, not only in regard to the wearing of sterile rubber gloves and gown and the boiling of all instruments, but also in regard to the always infected areas surrounding the orifice of the vagina. The escape of faeces is indicative of imperfect preparation on the part of the midwife, who should make sure that the big bowel is empty long before interference becomes necessary. In any case this is a small difficulty with which it is always possible to deal effectually before anything is done. The vulva must be shaved and the skin purified by means of one of the aniline dye or other preparations used for the sterilization of skin surfaces; and this purifying process must include the anal orifice, which is afterwards suitably protected before intervention is practised.

All this ritual is absolutely necessary; but is it possible for the unpaid, overworked practitioner? It will be said, I know, that thousands of forceps deliveries are effected daily without mishaps; yet 1.7 maternal deaths occur from registered sepsis—excluding phlegmasia and other conditions due to infection—in every thousand deliveries of live children.* How many mothers survive infection, perhaps permanently damaged, is, of course, unknown. This is a matter worthy of deep and serious thought. It is worth while, indeed, to consider whether interference should ever be practised in really unsuitable surroundings.

The time will come, I hope, when the Nation, and through the Nation the Government, will realize that parturition, especially when interference is necessary, cannot be conducted in rooms in which the accoucheur has to tuck his trousers into his socks—a tent in a public park would be infinitely better—and that, when interference is necessary, the practitioner must be awarded fees commensurate with the responsibility undertaken, the skill employed, and the cost of proper aseptic equipment, or equivalencies must be provided.

THE TREATMENT OF PUERPERAL INFECTIONS.

As I have already stated, probably a large majority of all cases of puerperal infection escape death, which still figures with such alarming frequency in the statistics of the Registrar-General, but certainly with deceptive relativity in regard to puerperal infections generally. This makes it obvious that the mortality rate would be much higher if it were unrelieved, not only by antisepsis, but also by the improved methods of treatment. It follows, therefore, that many opportunities are offered for the treatment of these cases, but I regret to say that, generally speaking, we have not made the best use of our opportunities, for cases of puerperal infection are unwelcome in maternity and surgical departments. In most large cities the patients find their way into the fever hospitals, where expert service is rarely available.

Infections of the Placental Site.

Most of us have come to regard sapraemia as a bacteriological refinement that should find no place as a term of

* Registrar-General's Report for 1919.

endearment in the disturbed conscience of the practitioner. The absorption of toxins produced by putrefactive organisms is, of course, not uncommon, and in such circumstances there is usually a foul discharge; but until streptococci and other pyogenic bacteria have been proved to be absent, as is rarely possible, they must be assumed to be present.

Infection of the placental site is always accompanied by pyrexia, an increased pulse-rate, and the other well-known signs of fever.

There is no commonly accepted morbidity figure, but a safe rule in regard to the necessity for active measures may be said to consist of the recognition of a rise of temperature over 101° F. on the second evening after the confinement. This should be a definite indication for intervention.

The uterine cavity should be explored with the gloved finger in order that any placenta which may have been retained may be removed digitally. In my opinion curettement, except with the finger, should never be employed. Some of the worst cases of puerperal septicaemia that I have seen have followed the use of a sharp curette. The uterus must subsequently be irrigated with a suitable antiseptic solution. I use Milton fluid, which is a powerful and stable hypochlorous acid preparation. It is advisable to use a strong solution of this fluid (1 in 10), which is hypertonic, for the first irrigation. Afterwards a solution of 1 in 30 will be found better, as the stronger solution is apt to be slightly irritating to the skin of the vulva.

A majority of all cases rapidly improve, some after one irrigation. This treatment may therefore be considered abortive in its action, and it is very efficacious in this respect. In the days past the solutions used were either poisonous to the patient or too weak antiseptically to be of much value, but even in these circumstances irrigation was found very advantageous—no doubt because the uterine cavity was cleansed mechanically.

If such treatment be delayed, or if in spite of such treatment the infective process continue, it is advisable, when thirty-six or forty-eight hours have passed without considerable improvement, for the practitioner to carry out irrigation more effectually by inserting into the uterus a double-tube—a large pattern similar to that which I use in the vagina after colporrhaphies—which may be fixed to the cervix with a stitch. With this tube in position the uterus can be irrigated very frequently without much discomfort to the patient.

When the lesion has become more than a superficial endometritis, serious surgical operations may be required. If there be localized abscesses in the uterine wall, the tubes or the ovaries, these structures must be removed, often at a fateful moment of selection.

Surgical interference is also, in my opinion—which, however, is not yet generally shared—the correct mode of procedure in cases of generalized septicaemia and pyaemia, if the condition of the patient and stage of the disease warrant operative intervention.

In general septicaemia without thrombosis of the pelvic veins the prognosis is extremely grave and the patient rarely recovers. Nevertheless, I believe that prompt ligation of the ovarian veins, which are easily accessible, and the internal iliac veins, cuts off to a considerable extent the general invasion of the blood. When the veins are definitely thrombosed and the patient has shown signs of pyaemia with a hectic temperature and corresponding rigors, the abdomen should be opened and the involved veins ligated and in certain circumstances excised.

I have practised this operation eight times in desperate cases with a fatal issue in two, in one of which the infection was with the pneumococcus. In two of the cases that recovered there had been aseptic emboli in the pulmonary vessels.

I have seen autogenous vaccines and polyvalent anti-streptococcal serum apparently do good in cases of acute general puerperal infections, but I think that while, whenever possible, they should be employed, the wise practitioner will not rely entirely on their efficacy in the present state of our knowledge. I have considerable faith in the intramuscular administration of 0.5 c.cm. of infundibulin (pituitary extract) extract every night and morning to maintain a proper blood pressure. I have, too, had one very happy experience in a case of streptococcal septicaemia of appendicular origin, which has indicated to me that

blood transfusion may be of temporary assistance to the surgeon in fighting a desperate condition.

Infections of Lacerations.

Cellulitis usually follows the infection of lacerations of the cervix and vagina. The condition may be acute or somewhat chronic in its course; it may commence acutely and become chronic. Patients may be invalidated for many months, and ultimately may be permanently affected by the lesions produced. Only occasionally does pelvic cellulitis prove fatal, and then because there has been failure to evacuate pus at the proper time. Cellulitis is easily discovered on examination of the patient, for the cellular tissue of the pelvis, especially of the broad ligaments, is involved, exudation follows and the uterus becomes fixed.

The treatment adopted in the early stages should consist of the sterilization, as far as possible, of the infected wounds, and the use of hot douches. If suppuration occur, drainage of the abscess cavity must be established.

Occasionally, however, septicaemia follows an acute streptococcal infection of a laceration. In these circumstances the treatment is confined to the purification of the wound and the employment of vaccines and serums, infundibular extract, saline infusions, and possibly of blood transfusion.

SUMMARY AND CONCLUSIONS.

1. There must be an honest recognition by all who attend childbirth that puerperal infection is almost always avoidable, and that the appearance of it in any case that has been examined, or in which interference has been practised, is a serious reflection on the accoucheur or accoucheuse. If the whole profession would combine in an attempt to reduce the present incriminating figures a great change would be noticeable, not only in the statistics presented by the Registrar-General, but also in the health of the female population which is perpetuating our race.

2. The remedy does not lie in better teaching, so far as practitioners are concerned, but in obedience to the dictates of conscience. No man can plead ignorance of asepsis and antiseptics to-day. The trouble is that imperfect asepsis is practised as a sop to conscience instead of complete asepsis as a real scientific safeguard.

3. Examination per rectum with the gloved finger should be practised in the case of the parturient woman in preference to vaginal examination. Forceps delivery is far too common. Most women deliver themselves safely if left alone. Forceps delivery, when necessary, is a surgical operation, and should not be conducted in insanitary surroundings.

4. All lacerations, not only those of the perineum, must be efficiently sutured.

5. Care must be taken to maintain the natural defences of the patient.

With regard to the treatment of puerperal infections the chief conclusions are:

1. The evacuation of large pieces of placenta and efficient antiseptic irrigation of the uterus should be practised in the early stages of infection of the placental site. All infected lacerations should be purified.

2. The employment of autogenous vaccines and polyvalent serums is often useful in cases of generalized infection.

3. Major operations must be performed, especially ligation of the veins in puerperal thrombo-phlebitis, without hesitation and in good time when indicated.

As to the more general considerations, the principal conclusions are:

1. Much research is required to define more accurately and fully the general and local defences against infection in the normal parturient woman, and the causes that lead to their diminution.

2. The immediate reception and accommodation of all cases of puerperal infection into a special ward connected with gynaecological and obstetrical clinics, where each can be adequately investigated and efficiently treated, should be possible.

3. Aseptic midwifery is prohibitively costly to the general practitioner in comparison with the fees obtaining

in the poorer parts. In every district a dépôt should be established by the local authority from which the general practitioner could obtain a sterile outfit free of cost.

4. The present statistics are an urgent indication that better organization is required. In various centres, especially in industrial districts, large maternity and gynaecological clinics should be instituted. When possible they should be attached to the teaching schools. These clinics should form base hospitals for wide areas, in the outlying parts of which a few beds should be set aside in existing cottage hospitals, or, failing these, small field hospitals should be established for the reception of maternity cases. In these field hospitals general practitioners would have an opportunity of working under the best conditions when interference was necessary. In cases of special difficulty skilled assistance could be summoned from the base hospital, if the patient were too ill to be moved. Whenever difficulty was anticipated the patient could be sent before the commencement of labour to the base hospital for delivery.

Remarks

ON

THE USE OF PEPTONE IN ASTHMA AND ITS CONGENERS.

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THESE remarks have been largely prompted by the numerous inquiries and requests for further information received since my last paper.¹ Any new treatment necessitates a long period of probation; it must be tested and retested in a large number of cases, and the results scrutinized in the light of any criticisms which legitimately may be raised. It is satisfactory, meanwhile, to be able to state that the reports from many sources, both home and foreign, are such as to justify the general conclusions previously recorded. The treatment has been applied not only to asthma, but also to such of its congeners as hay fever, associated skin affections, angio-neurotic oedema, cyclic vomiting, periodic diarrhoea, and the migraine-epilepsy syndrome; in short, to such conditions as exhibit an anaphylactic character or sensitization.

The Scientific Basis.

The discussion in my previous papers as to the scientific grounds of the treatment had, as its pivot, the identical characters of anaphylaxis and peptone poisoning or shock. But, notwithstanding the arguments employed and the clinical results, it was difficult for many, and especially for those practically acquainted with experimental anaphylaxis, to believe that a substance (peptone) which had lost its specificity, and could functionate no longer as an antigen in the strict sense, was nevertheless capable in small doses of counteracting the effects of a specific antigen. I took the view that the immunizing action of the peptone was directed, not against the antigen itself, but against the antigen-antibody product. This product, by its interaction with the cell-protoplasm, is the cause of the anaphylactic shock, which is identical with the shock produced by the interaction of peptone and the cell-protoplasm. It is usually believed that a substance of great potency, such as histamine, results from this reaction. That there is also a violent dislocation of the colloidal equilibrium of the blood and cells by a coalescence or aggregation of particles is likely, and is even regarded by some as a sufficient explanation of the phenomena. As bearing on this, mention may be made of some clinical experiments (not yet completed) which I made with lecithin. In the course of these I observed that a bile salt solution of the purest lecithin obtainable,* intravenously administered, seemed to exert a more or less inhibitory effect on the anaphylactic reaction. As both bile salt and lecithin reduce the surface tension, their action would be directed against the coalescence of colloidal particles by stabilizing the electric double layer. Possibly it is in this direction that the inhibiting action of narcotics is to be sought.

* Most commercial lecithins are grossly contaminated, and give rise to toxic symptoms.

It appeared to me that the case for the clinical use of peptone might be well served by animal experiments, so some little time ago I put the matter before Dr. H. H. Dale, and urged him to carry out some experiments with small doses of peptone in relation to anaphylactic shock in sensitized animals. This he kindly agreed to do, and lately I received from him a preliminary report in which he says, "The results are definite enough. A dose of peptone not itself large enough to produce any pronounced reaction, will weaken the response of a sensitized guinea-pig to the sensitizing antigen, so that after such a dose it is possible to desensitize without at any time producing any pronounced reaction. This I think ought to be valuable." . . . "The specific desensitization would appear, in part at least, to be due to the detachment of antibody from the cells."

As Dr. Dale intends to have the matter more fully investigated, it is sufficient to remark that as it has now been proved experimentally that peptone in small doses can inhibit the anaphylactic shock, its clinical use in conditions of sensitization has been placed on a solid foundation. Previous experiments with peptone in this connexion were made with massive doses and the results were conflicting. But one usually finds in experimental work that the effects of small doses are not sufficiently studied.

Now this active immunity or desensitization produced by peptone is a totally different process from immunization as ordinarily understood and practised. The immunity produced by a bacterial vaccine or a native protein is associated with the production of antibodies which are stereochemically fitted to the particular antigen and to no other, although there is a certain amount of overlapping in nearly related antigens. These antibodies when circulating in the blood dispose of the antigen, but if they are attached to the tissue cells and the antigen gains access to them, shock results. Peptone forms no such antibodies. When the protein molecule is reduced to proteoses and peptones, its specific architecture is practically obliterated, so that the immunizing action of peptone is independent of the nature or configuration of the antigen. It is a desensitizer in the general sense, though possibly more effective against some antigens than others. Dale, as is seen, thinks that this action on the part of peptone is, partly at least, such as to lead to detachment of antibodies from the cells. They would thus become free in the blood, and destroy or render innocuous the antigen.

Nature and Effects of Sensitization.

It was recognized by our forefathers that heredity and a family relationship were frequently encountered in those disorders which we may now reasonably regard as expressions of sensitization. Recent observations (R. H. Cooke and Van der Veer,² Freeman,³ Buchanan,⁴ etc.) have more fully set out these relationships, in which some have found strong evidence of the operation of the Mendelian law. If sensitization, potentially considered, implies the segregation of determinants in the germ plasma and is transmitted as a dominant factor, much that was obscure becomes luminous. The transmission may not be the particular sensitization but an abnormal susceptibility to form antibodies to foreign proteins, a "vice of nutrition." As regards the nervous system, Buchanan's studies lead him to conclude that the migraine factor is the transmitter, as 75 per cent. of essential epileptics have a migrainous strain. Possibly the rare disease "family periodic paralysis" is also an example of sensitization in which the antigen attacks the mechanism of inhibition.

The earlier the symptoms appear the stronger as a rule the inheritance, which may be double. On the other hand, failure to elicit a positive history is by no means conclusive, as no adequate study of the heterozygotes may have been made in relation to recessive unit characters. The clinical symptoms depend on the locality of the sensitized cells, and it is also likely that the offending protein has a predilection for certain parts or cells. Very often the whole body seems to take a sympathetic part in relation to the sensitization of a particular structure, while in other cases the sensitization seems practically confined to a limited area. In this relationship, cutaneous tests, though in some cases definite enough, play tricks with us, and their full significance is very far from being understood. This is forcibly brought out in the writings of Schloss, Smith, Longcope, Highman, Wells, and others. In some cases