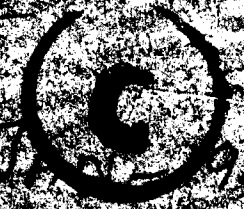


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Vol. XI.

JANUARY 1942.

No. I.

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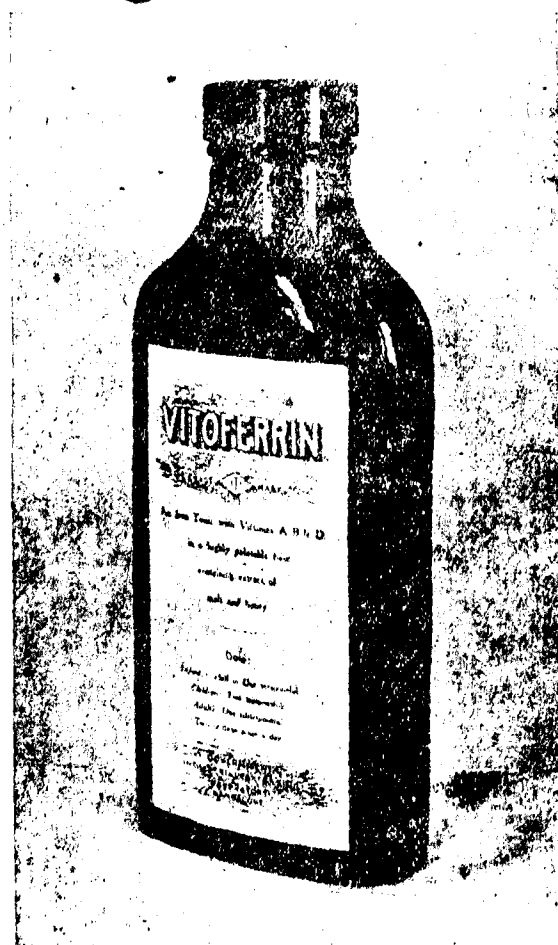
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## MEDICO-SURGICAL SUGGESTIONS

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### REPAIR OF THE PERINEUM UNDER LOCAL ANAESTHESIA.

BY BRYAN WILLIAMS, M.D., M.R.C.O.G., F.R.C.S.E.

Repair of the perineum after delivery is one of the commonest operations that a practitioner is called upon to perform, and it is the purpose of this article to show that the great majority of these tears may be adequately sutured under local anaesthesia by the single-handed practitioner under even the most difficult surroundings.

Local anaesthesia by infiltration is the anaesthetic of choice in most cases in domestic practice, as well, indeed, as in hospital practice. Its safety for cases of cardiac diseases, or where there is shock, is obvious. In normal cases also, however, it should be more generally used, and in nearly every case, with time and patience, good results can be obtained. The few cases in which it is unsuitable are those in which the patient is very nervous or will not co-operate and remain still in the lithotomy position, a few cases in which the tear is very high or extensive and in which much retraction is necessary, and those cases in which a complete perineal tear is present. In such cases some other form of anaesthesia, such as spinal or general, is necessary. As the result of an experience of a large number of repairs carried out under local anaesthesia, both in hospital and domestic practice, often in extremely unfavourable surroundings, the following technique is recommended.

#### TECHNIQUE.

No elaborate armamentarium is necessary. While special local anaesthesia syringes are helpful, good work can be done quite satisfactorily with a record syringe, most conveniently of 10 c.cm. capacity. Two sizes of needle are necessary with this—a fine hypodermic needle and a fairly long serum needle. After trying various anaesthetics in different strengths, I have found that a 1 per cent. solution of novocaine, or equivalent preparation, without adrenaline, to be the most satisfactory one. Stronger solutions are unnecessary, and weaker solutions require an undesirably large

volume to produce anaesthesia. The amount required will, of course, vary, but a minimum of about 10 c.cm. will be required for small tears.

The instruments used will depend on the preference of the surgeon. Usually small round-bodied curved needles with a needle holder are most convenient for the mucous membrane and deeper tissues, and these should be strong, as otherwise it is very easy to break them during the insertion of sutures, with awkward results. A combined needle-holder and suture cutter, such as that described by the author (*B.M.J.*, 1940, 2, 227), is of great help when one is working single-handed. For the skin, a large cutting needle is necessary. A small handled needle is useful for the deeper tissues, but the giant perineum needles illustrated in the catalogues are quite unnecessary. Size 2 catgut is the most suitable, and owing to the rapid rate of healing after delivery, this may be of the plain variety.

The left lateral position is quite unsuitable for the adequate inspection and repair of tears. The dorsal position, now becoming more general in this country for abnormal obstetrics, is the only satisfactory one, and may be maintained by quite simple methods. In domestic practice, the patient may be placed across the bed, with the buttocks well over the edge, and the feet resting on chairs. The simple device known as the "obstetric helper" may also be used. This is a simple trap which passes round the patient's neck and over her shoulders, and buckles in a convenient manner round the thighs. It is comfortable to the patient and can be washed. Most patients will co-operate in the maintenance of the dorsal position, but if unfortunately they will not, then a local anaesthetic cannot be used. Good light is necessary, and should come over the operator's shoulders. If both daylight and artificial light are inadequate, and this is much more likely nowadays with the black-out, a simple headlight worked off a dry battery is extremely useful.

Thorough mechanical and antiseptic cleansing of the field must first be undertaken according to the operator's usual technique. It must be remembered, however, that the raw tissue may be extremely sensitive to both chemical and mechanical stimuli, and must be dabbed with extreme gentleness. All swabbing must be carried out from before backwards, and the swabs then discarded. The legs and the operation area must then be covered with sterile towels, but quite satisfactory work can be carried out in domestic practice without these if a strict antiseptic and aseptic conscience has been achieved.

A full inspection of the laceration must now be made. The importance of this cannot be overestimated. It is not always realized, especially by midwives, that the skin of the perineum may

be intact, while internally there is an extensive laceration of the deeper tissues. On the other hand, the skin alone may be torn back to the anal margin and gives the appearance of a complete tear, without there being any serious deeper tear. There are two important signs which nearly always indicate perineal laceration. These are oedema of the perineum, and laceration of the labia minora. These labial lacerations should be looked upon as "sentinels" indicating a more extensive tear posteriorly, into which, indeed, they often run. These labial tears, even if small, should always be sutured, as otherwise a painful raw area may be left, and adhesions between the two sides may occur.

Most tears will be found to have a diamond-shaped appearance, but there is great variation in their extent and appearance, as well as in the local anatomy. Tears are more common to one side of the mid-line, and may at first be hidden in a vaginal sulcus. Occasionally H-shaped, U-shaped, or M-shaped tears may be found. Sometimes an extensive laceration, more deserving the term "burst vagina," may be found. This occurs when the vulva is very small and rigid, when there is great disproportion between the presenting part and the soft tissues, when the accoucheur's hand has been introduced into the vagina alongside the presenting part, or when there is a contracted outlet or narrow pubic arch. In such cases there may be great separation of the mucous membrane from the perineal body and skin, and an extensive raw area is left which is very difficult to repair anatomically. Very rarely there may be an intact bridge of skin anteriorly with a tear behind, the "central tear" of the perineum. Occasionally an anterior tear may almost seem to expose the pubic bone, which can be felt by the palpitating finger with great ease. Most of these extensive lacerations should, of course, have been prevented by an episiotomy, and this may well be carried out under local anaesthesia. The extent of the tear may often be more certainly determined by digital palpation than by inspection.

If the repair is carried out some time after delivery of the placenta, there will usually be little bleeding, especially if care is taken previously to express clots from the uterus. If there is a slight bleeding, a pack placed in the vagina will keep the field clear, but if this is done, a forceps or suture must always be left attached to the pack, as otherwise it is extremely easy to forget its presence in the vagina at the end of the operation.

Throughout the whole procedure, the psychical aspect of the case must always be borne in mind, and much of the success of the anaesthesia will depend on how this is dealt with. The surgeon will have learnt much if he has ever had any operation under local anaesthesia, such as a dental extraction, performed upon himself. He will also learn much from carrying out operations under local

anaesthesia. An increased respect for tissues and a greater delicacy of touch are taught by its use.

The patient will remain sensitive to touch and traction, and unless this is explained to her, she will get the impression that the anaesthesia has failed. It is also advisable for the surgeon or someone else to talk to her during the procedure. Post-partum cases differ from other surgical cases in that the greater part of the ordeal is now over, and the patient is more or less happy, and will talk readily of her baby and her family. This aspect of the case cannot be over-emphasized, and if attention is paid in this direction, sufficient time spent over the case, and the infiltration adequately made, failure will be very rare.

Injection of the anaesthetic should be commenced with the hypodermic needle. This is entered from the raw area immediately under the skin, and the solution is injected very superficially, or even intracutaneously. The raw area is seldom sensitive to the passage of the needle, but if desired, a swab soaked in the anaesthetic solution may be applied to its surface for a few minutes. The skin on each side of the tear is carefully infiltrated, at first with the hypodermic needle, and then with a longer serum needle. It is most important that the skin in the posterior part of the tear, especially if this is near the anus, should be well infiltrated, as this is extremely sensitive. A superficial injection of any labial tears should then be made, and it should be remembered that the skin in this region is very sensitive. A small amount should next be injected into the perineal body. This is moderately sensitive to traction, but less so to other kinds of stimuli. It must be remembered that after delivery the soft tissues of the pelvis are very lax, and that much more fluid can be injected than in normal tissues. It is not necessary, however, that the tissues should be ballooned out, as is usually done in infiltration anaesthesia with weak solutions, but only that an adequate amount should be used in the sensitive parts. In cases of toxæmia and heart disease there will often be vulval oedema, but this does not greatly interfere with the effect of the anaesthetic, and it is often in such cases that we wish to obtain the advantages of local anaesthesia.

The mucous membrane itself is not sensitive to the passage of a needle, but a small amount should be injected into the mucocutaneous junction. The repair may then be commenced, and it will be found that by the time the skin has been reached, there will have been time for the anaesthesia to be complete.

The method of repair differs in no way from that adopted by the surgeon when other kinds of anaesthesia are used, and the details will depend on his usual technique. The general principles are that the tissues should be accurately brought together, that no dead spaces should be left, and that the minimum of foreign material

should be buried. Catgut is the most satisfactory suture material. It does not require to be removed, and is less painful than silkworm gut for the skin. Silkworm gut of medium thickness, however, is useful for small lacerations, and is of special value for the figure-of-eight stitch to be described shortly. Interrupted sutures should be used throughout, as they are more reliable, though not so haemostatic or so quick to insert as continuous sutures.

Sometimes it is difficult to reach the top of a laceration, and this is especially the case with an episiotomy that has extended high up the vagina. In such a case, it is helpful to insert a single suture in the mucous membrane as high as possible, and to use this as a traction suture to pull down the mucous membrane, which usually has considerable mobility, and thus expose the higher part of the tear. Even with this aid, however, it is sometimes necessary to insert the highest suture by touch.

Interrupted sutures are then inserted in the upper part of the mucous membrane tear. A good bite of tissues should be taken, though care is always necessary near the mid line in high tears, as the mucous membrane of vagina and rectum are here close together. The mucous membrane repair must not be completed, however, until the deeper tissues have been brought together, as otherwise a dead space will be left.

The levators and the perineal body are then brought together with deep sutures, and it is convenient to insert these with a handled needle. A good bite must be taken, but again extreme care must be used in the mid-line to avoid entering the rectum, as this is very easy to do when the perineum is short. The needle should be inserted rather parallel to the mucous membrane than at right angles to it. It is probable that a stitch entering the rectum is the cause of many poor results, or even of recto-vaginal fistulae. All dead spaces should be obliterated when the sutures are tied, and the catgut should be cut close to the knot in order to leave the least possible amount of buried material. The figure-of-eight stitch is of great value at this stage. This takes first a bite of the mucous membrane on one side, then of the deep tissues on the opposite side, then of the deep tissues on the first side, and finally emerges again through the mucous membrane on the opposite side. This stitch brings the deeper tissues well together with the minimum of buried material.

The lowest part of the mucous membrane is then brought together, and finally the skin is sutured. A cutting needle is necessary for this. It is unnecessary to insert the stitches closely. Care must be taken, however, to evert the skin edges, and not to tie the sutures too tightly, as they may be very painful if there is any subsequent oedema. Silkworm gut stitches should be cut short, as otherwise the ends may stick in the patient and be very painful.

Alternatively they may be left fairly long and the ends tied together and enclosed in a swab.

A rectal examination should always be done at the end, and the bulk of the perineal body and sphincter palpated between finger and thumb. In this way the soundness of the repair and the adequacy of the sphincter will be tested, and the presence of any suture in the lumen of the rectum detected. If unfortunately this is found, the gloves must be changed, the whole repair taken down, the field cleaned, the offending suture removed, and the repair carried out again.

No special after treatment is necessary. If there is any oedema, a glycerine dressing is comforting. The patient should not be kept constipated, as I believe the disadvantages of doing so outweigh the supposed advantages, even in complete tears. Silkworm gut stitches may be removed in eight to ten days, or even earlier if healing is good. It is also sometimes advisable to remove catgut sutures, as absorption is often slow, and the knots collect discharges.

(*"The Postgraduate Medical Journal," July, 1941.*)

## PREVENTION AND TREATMENT OF INFECTION OF THE HAND.

BY SUMMER L. KOCH, M.D.

Recently I had an opportunity to summarize the results of treatment of all open wounds sustained by the workers in a manufacturing plant located approximately a mile from the hospital with which I am affiliated. The number of injuries was not large—sixty-nine in a period of sixty years—and the injuries were not often serious, consisting for the most part of clean-cut wounds resulting from the handling of metal sheets and strips. There were included, however, a number of cases in which division and suture of digital nerves were necessary, one case in which division of flexor tendons was done, and two in which division of extensor tendons was done. The rules for the care of injuries were simple and definite—a sterile dressing was to be applied immediately over the open wound and the injured employee taken to the hospital without delay.

The majority of these patients were seen within a half-hour of the time of injury. At the hospital the open wounds were carefully cleansed with plain white soap and sterile water applied with soft, sterile cotton and gloved hands were irrigated with warm salt solution by a resident or a surgeon carefully masked and scrubbed before he began cleansing the wound. The cleansed wounds were

immediately repaired and closed. If loss of covering tissue had resulted from tangential wounds a graft of skin was applied immediately. Anaesthesia was often secured with a 0.5 per cent. solution of procaine hydrochloride and sometimes with nitrous oxide.

The fact that stood out was that of all the patients, 47 in number, who were sent to the hospital immediately after the injury of only one failed to heal by primary union and without infection. In one patient with a crushing injury and a subungual haematoma a low grade infection developed underneath the nail. Twenty-three cases in which infection occurred were seen during the same period. In every case except the one just mentioned the employee had failed to report until an average period of three days after the injury, and in every case definite signs of localized or spreading infection were present when the patient was first seen.

Of 41 patients reporting immediately after the injury, including the one in whom infection developed, the average loss of time from work was 2.2 days. Of six workers reporting immediately after injury, three with fractures of fingers or toes (two with compound fractures) and three with division of nerves and tendons, the average loss of time from work was 29 days. In these cases, furthermore, healing occurred by primary union, but the necessity for prolonged immobilization after fracture of bones, tendons or nerves was responsible for the delay in returning to work.

Of the patients who reported at intervals varying from six hours to eight days after injury, and who showed evidence of infection when first seen, the average loss of time was 11.1 days, raising from no loss of time from work to periods of 28 and 32 days, the two longest intervals.

In none of the cases that were seen and cared for immediately after the injury was sustained and in none of the cases of extensive compound injury was sulphanilamide or any of its derivatives or any so-called antiseptic used at any time during the course of treatment.

The moral, I think, is clear. The most certain way to prevent infection of an open wound is not to fill it with tincture of iodine or sulphanilamide crystals, but to cover immediately with a sterile dressing and entrust the patient to someone who will give him cleanly surgical care without adding further contamination to the open wound. With increasing experience physicians are coming to realize that the most important source of contamination of an open wound is not the metal or knife or glass that caused the wound, not the bacteria that may be present on the patient's skin, but the uncovered noses and mouths of excited by standers, or first-aid workers, or of anyone who is attempting to examine or treat an open wound without carefully masking his face, covering his scrubbed hands with sterile gloves, and making certain that the instruments and materials with which he is working are sterile. Uncovered

mouths and noses, hands hastily scrubbed and instruments dipped for only a moment in an antiseptic solution are the real sources of the infection that the thoughtless workers so often considers the inevitable sequela of an open wound.

I would not decry the value of chemotherapy when it is indicated or deny for a moment that the sulphonamides are of great help in combating and arresting certain types of infection. The point I would stress is that the first line of defence lies in the immediate protection of the open wound so that infection from without is not permitted to enter, and the next line, in simple surgical cleanliness that does not add chemical and mechanical trauma to the fragile, delicate cells of living tissue.

Once infection has developed in an open wound the surgeon must first answer the question "Is the infection diffuse and spreading or is it localized?" Why? Because diagnosis must precede rational and effective treatment, and the treatment of the two types of infection is radically different. The acute, spreading infection requires absolute rest, application of warm, wet, sterile dressing to help nature mobilize the defensive forces of the body and brings about localization of the infection, specific chemotherapy and abstinence from any form of active surgical intervention until localization is secured. If a localized infection is present, in other words if an abscess has formed, the sooner the abscess is drained the sooner will the continuing necrosis that is synonymous with infection be arrested and the inauguration of healing made possible. Both types of infection obviously demand all the means at the disposal of the surgeon for building up the resistance of the patient and neutralizing the harmful effects of virulent organisms.

If an infection is localized, and these principles apply as definitely to every part of the body as they do to the hand, the next question is again one of diagnosis: Where is the infection localized?

Paronychia, felon, collar button abscess, infection of the lumbrical space, subfascial infection, infection of a tendon sheath, infection of thenar, middle palmar or subaponeurotic space all are definite clinical entities, with clearcut and unequivocal symptoms. For each there is one best method of securing adequate drainage which will lead to healing in the minimum period of time and with minimum injury and loss of function.

Space does not permit, nor is it necessary for me to repeat here, the detailed symptoms or treatment of the various types of infection of the hand. I would like, however, to stress a few general principles which apply to the surgical treatment of every form of localized infection.

The preparation of the field of operation should not cause pain or add injury to tissues already devitalized by infection. I know of no better method than the gentle and patient cleansing with soap and

water that I use in the care of an open wound which has just been sustained. Everyone has seen the destructive effect of chemical antiseptics, for example, of tincture of iodine, on inflamed and injured tissues.

A general anaesthetic is preferable to a local anaesthetic, because it does not add further injury to the injured tissues, and because it permits the surgeon to work with the deliberation and care that are synonymous with "good surgery." The opening of an infected tendon sheath, for example, involves careful exposure and complete visualization of the digital nerve on the side the finger chosen for incision. If the digital nerve is exposed and retracted dorsal there can be no question of injuring digital blood vessels, for they lie dorsal to the nerve. The tendon sheath, though it may be filled with pus, is a relatively small tubular structure. The diffuse swelling of the finger which always accompanies infection of a tendon sheath results from the cellulitis of the distensible, soft subcutaneous tissues outside the sheath, although the "abscess" is within the synovial sheath. Not infrequently one sees an infected finger in which the soft tissues only have been incised and the sheath within which the pus is held remains unopened. Such failures and irreparable injuries of essential nerves, blood vessels, and tendons themselves can easily occur if the watchword of the surgeon is "Get in and get out."

A bloodless field is an invaluable asset for careful and exact surgical procedures. It is an easily available boon for the surgeon working on the extremities. Before any operation is carried out on the hand a blood pressure cuff is applied to the patient's arm and a bandage wrapped smoothly around it so that a part of the rubber bag cannot escape from underneath the bandage as the cuff is inflated. Just before operation is begun the extremity is raised for a few moments and the bag inflated with a pressure of 250 mm. of mercury. A bloodless field permits the surgeon to make accurate incisions, to make certain that important structures are left uninjured and that the infected area is adequately and effectively drained. One single observation that attests the importance of accurate visualization of the field of operation is the not infrequent occurrence of infection of a tendon sheath resulting from incision for drainage of a felon. Such a complication should never occur, but if one is attempting to make a quick incision in a distal phalanx obscured with blood and for a patient who is scarcely able to tolerate the pain in the acutely inflamed and incompletely anaesthetized finger, it is not difficult to go beyond the anterior closed space and carry infection into the vulnerable tendon sheath, as it surrounds the flexor profundus as its insertion on the base of the distal phalanx.

After an adequate incision has been made to drain the affected area, the tough and rigid edges of skin must be held apart for

twenty-four to forty-eight hours so that they do not promptly become agglutinated and prevent escape of infectious material. A soft wedge of gauze saturated with petrolatum and placed in the angle of the wound where it will be least likely to obstruct drainage is the best method I know. Too often what is called a drain is simply a cork, and serves only to dam back exudate rather than to aid its escape.

Incisions on two sides of a finger or hand are almost never indicated. Unnecessary multiple incisions simply require a longer period for healing and tempt the surgeon to insert drains through the finger or palm—the most certain and effective way of causing necrosis of vulnerable tendon sheaths and tendons.

Drains can invariably be removed in twenty-four to forty-eight hours, and should not be replaced. There is no more certain method of adding infection to an open wound and of delaying the healing process than by repeated reinsertion of "drains." If the incision for drainage is adequate and correctly placed, spontaneous drainage will continue until healing takes place; if it is not, continued reinsertion of a drain will not compensate for the error.

Immediately after an abscess has been drained the continuous application of external heat over a moist sterile dressing for two, three or four days favours drainage, stimulates the circulation, and relieves pain. If the extremity is elevated, the return circulation is aided and the onset of congestion, delayed. Continuous application of warm wet dressing should not be continued indefinitely. The onset of congestion, with its resultant maceration of covering tissues and oedema of deeper tissues should be anticipated by substituting for the continuous moist dressings, three or four days after operation, intermittent soakings in warm sterile solutions followed by drying of the extremity under a heat lamp.

Throughout the post-operative course every effort should be made to dress the injured hand with cleanly surgical care, and avoid adding further infection to that which has already occurred.

Finally, the important principle of providing rest for the injured tissues should be constantly kept in mind. Light aluminium splints, which can be easily fashioned into desired shapes, and which can be sterilized and incorporated into the dressing from the outset of treatment, help greatly to provide the rest that aids healing and brings relief from pain.

("Journal of the American Medical Assn.," March, 1941.)

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## EPILEPSY.

BY DONALD MCEACHERN, M.D.

Epilepsy is a symptom and is due to periodic and abnormal neuronal discharge in the brain. Each one of us is a possible candidate for an epileptic seizure under certain circumstances. Temporary arrest of blood supply to the brain, hypoglycaemia, a sufficient dose of some convulsant drug, or other factors might induce a seizure in any normal person. In a sense the epileptic seizure is the brain's normal response to certain abnormal circumstances. The trouble is that in many cases of epilepsy we do not know what the abnormal circumstances are.

In the end such neuronal explosions must be due to metabolic or physico-chemical changes in nerve cells which render them unstable and permit them to fire off either spontaneously or when disturbed by a scar, a tumour, or other abnormality of the brain.

Our main clinical problems are: (1) to recognize and treat those cases in which seizures are due to disease of the brain, or to abnormalities of the circulation or of the chemical processes of the body; (2) to treat symptomatically the cases which in our ignorance we label "idiopathic" epilepsy.

## INVESTIGATION OF A CASE OF EPILEPSY.

The revelation of an organic cause in cases thought to be "idiopathic" epilepsy is sufficiently common to suggest that all patients should have the benefit of complete study early in their epileptic careers.

*Clinically*, the age of onset and type of seizure are of fundamental importance. Omitting the convulsions which occur so frequently in childhood associated with any fever, we may say generally that epilepsy commencing within the first two decades usually is to be placed in that vague group called "idiopathic." Commencing within the next two decades it is usually associated with cerebral tumour. Thereafter renal and cerebral vascular causes become increasingly frequent, but the possibility of cerebral tumour should always be borne in mind. A history of prolonged or difficult birth and retarded development may indicate cerebral birth trauma. Head injury, even if remote, should suggest the possibility of a meningocerebral scar as a cause of seizures.

Every physician, nurse, and relative should be schooled to describe accurately the patient's aura and the pattern of attacks. It is essential to observe the very beginning of an attack since it may rapidly spread from a focal to a generalized convulsion without localizing pattern. Rapid examination immediately after an attack may reveal temporary changes in the reflexes or sensibility which point to a focal defect and which cannot be elicited in the interim.

It is occasionally necessary to induce an attack in order that the pattern can be determined. This can sometimes be accomplished by having the patient hyperventilate until an attack occurs or until carpopedal spasm appears. Hydration of the patient is even more effective. Water is given in large quantities along with repeated injections of pitressin. This is however a hospital procedure.

Appropriate chemical studies are based on the circumstances under which attacks occur. Spontaneous hypoglycaemia may be suspected if attacks occur during fasting and are preceded by vagueness, anxiety and sweating. Attempts should be made to produce attacks by fasting, to relieve them by administration of glucose, and to obtain chemical proof by blood sugar determinations made during attacks. Glucose tolerance curves should be carried at least to five hours in order to determine the low point which follows the early rise of blood sugar.

We have seen two elderly patients recently in whom epileptic seizures occurred only during the development of recurrent latent tetany. One suffered from osteomalacia, and the other from mild parathyroid deficiency resulting from a thyroid operation. Attacks associated with uraemia, cerebral syphilis, vascular hypertension, and cerebral arteriosclerosis are usually recognized by careful routine examination. Even in these instances however special studies may be necessary, since there is no guarantee that cerebral tumour and arteriosclerosis or syphilis do not co-exist. We have seen the conjunction on several occasions.

Mention should be made of seizures in people with hypersensitivity of the carotid sinus reflex mechanism. As a result of sudden turning of the neck, an unusual position of the head, or the pressure of a high stiff collar, such patients suffer from a reflex fall of blood pressure or cardiac arrest, or both. Syncope results, and if the cerebral circulation is interrupted for more than about 12 seconds a convulsion may ensue. One of our patients, a middle-aged man, consulted Dr. Wilder Penfield because of the occurrence of seizures since childhood. Attacks first came when he knelt to pray in church on Sundays. This was the only day of the week when he was dressed in an Eton suit with high stiff collar. Attacks ceased when the minister advised that he may stay away from church since the prayers obviously did him no good. Attacks recurred later when he sat in the barber's chair and his head was thrust toward while the nape of the neck was clipped. It was easy to reproduce the attacks by light pressure over either carotid sinus. Explanation of the mechanism may suffice to keep these people out of trouble. Atrophine or ephedrine is occasionally helpful. If necessary the sinus can be denervated surgically. Attacks of similar character occur with Stokes-Adams syndrome.

*Roentgenography*.—Good stereoscopic X-ray films of the skull should never be omitted. They may show quite unsuspected bony changes or asymmetry of the skull. There may be calcium deposits indicative of tumour, shift of the shadow of the pineal gland due to an atrophic or expanding lesion in one hemisphere, or even evidence of increased intracranial pressure.

*Pneumography*.—X-ray visualization of the ventricles following injection of air or oxygen into the subarachnoid space has proved an invaluable procedure. When there is no contraindication once-phalography is done, the gas being injected by the lumbar route after removal of spinal fluid. In the case of a girl of 8 who had been presumed to suffer from idiopathic epilepsy for 4 years, X-rays of the skull showed marked disproportion between the two sides of the cranial cavity and the encephalogram revealed lack of filling of the right temporal horn and displacement of the ventricles to the left. At operation a large cystic collection of cerebrospinal fluid was found in the right temporal lobe due to a thin membrane which separated the temporal horn from the rest of the ventricular system. This thin veil of tissue, presumably a congenital defect, spelled the difference between normal health and epilepsy for this patient.

In another case, a man of 46, whose only complaints were two generalized convulsions commencing several months previously, clinical examination was negative. The encephalogram showed the right lateral ventricle to be depressed downward and displaced to the left. This was due to a large meningeal tumour which was removed completely.

Meningocerebral scars, subdural haematomas and areas of focal atrophy may also be recognized by this method and dealt with surgically.

*Cerebral arteriography*.—The visualization of the cerebral arteries following injection of a radio-opaque substance, such as thorotrast, into the carotid artery in the neck is of limited usefulness. When an aneurysm or vascular tumour is present, however, it may be the best or the only way to visualize the lesion. This was well shown in arteriogram of a man of 29 who suffered from Jacksonian seizures in the left arm. An arterio-venous aneurysm was visualized in the right parietal region and later removed by block dissection.

*Electroencephalography* is a newcomer in the field, but has already established itself. During its few years of rapid growth this ingenious method of recording the electrical potentials of the brain has emerged from the stage of pure experiment, and has become a reliable clinical tool. It is already in routine use in a number of large hospitals. The Department of Electroencephalography at the Montreal Neurological Institute, under the direction of Dr. Herbert Jasper, carried out 1,104 such examinations on 627 patients during the past year.

The principle of the method is that the rhythmic changes of potential of the normal brain can be led off from the surface of the intact scalp, stepped up about one million times by radio amplifiers, and recorded by means of ink writers on a moving strip of paper. Small silver electrodes are fixed to the scalp with collodion in a number of standard locations on each side of the head. These are led off to a switching box which permits simultaneous records to be made from a number of locations. The electrical activity of one side of the brain may be compared with that of the other side, or one small area with another.

Normally, two main rhythms can be recorded from the adult brain. Alpha (Berger) waves appear from the occipital regions at a frequency of about 10 per second, and beta waves at about 22 per second from the frontal regions. In epilepsy the normal rhythms are greatly disrupted, not only during a seizure but nearly always during intervals when the patient seems entirely well.

The following are some applications of this method to our knowledge of epilepsy.

The *diagnosis* of an epileptic attack can usually be made on clinical grounds when a seizure is observed or has been accurately described. When, however, there is but a vague history of fainting spells, of waking in the morning with a bitten tongue, or of momentary absences, the diagnosis of epilepsy is a precarious one. The electroencephalogram may assist by showing either typical epileptic abnormality or a normal rhythm. Further, temper outbursts and fleeting personality changes in an epileptic patient can sometimes be correlated with a surge of subclinical electrical abnormality in the brain, although there may be an outward sign of a convulsive seizure. Indeed many problem children have been found to have such electrical abnormalities although they had never suffered convulsive seizures.

There is also some indication from the record of the type of epileptic activity. Gibbs and his associates have described three distinct types of electrical abnormality which they think fit clinically with grand mal, petit mal, and psychomotor seizures. This relationship holds frequently but not always. It is possible that with further experience we will classify seizures according to the underlying electrical abnormality, just as the terminology of the cardiac arrhythmias was altered by MacKenzie's study of pulse tracings and Lewis' analysis of the electrocardiogram. Jasper and Kershman have already offered a tentative classification on electrographic lines.

Occasionally, differentiation between hysterical and epileptic seizures may be aided. Records taken during an hysterical seizure show a normal cerebral rhythm. Epileptics always show seizure waves during an attack.

*Localization of epileptic foci* is an important function of electroencephalography, and when this evidence coincides with clinical and pneumographic evidence, it often leads successful surgical removal of the focus. Localization is accomplished by determining the point between two sets of electrodes at which the abnormal electrical waves reverse direction (phase reversal).

Finally, the method may be of value in the *control of medicinal therapy*. If a patient has a seizure only once in months it may take painfully long to determine whether his medication is adequate. He may, however, show almost continual epileptic activity in the electroencephalogram which becomes reduced or disappears within a few days with adequate therapy. Unfortunately, there is no rule to this and some patients may remain free of attacks with little or no improvement in the electroencephalogram.

This method can be employed also to recognize lesions which are not epileptogenic. Thus subdural haematomas, tumours or infarcts of the brain may be localized by the damping down, the alteration or absence of normal brain potentials in a certain region. Electroencephalography has much to offer us and will contribute much more in the future.

We have reviewed the steps sometimes necessary to uncover the causes of epileptic seizures, but there remain many cases for which no cause can be found. It is worthwhile therefore to discuss the medicinal treatment of such cases.

#### TREATMENT.

*Drug therapy.*—We will consider here only four drugs of proved usefulness—the bromides, phenobarbital, dilantin and mebaral.

The bromides are used much less now than formerly. They are often not as effective as the other drugs. They frequently cause unpleasant acne, depress and slow down the patient's mental activity, and occasionally pile up in the system to cause a real toxic psychosis. The latter picture is not as well known as it should be, although it is not uncommon. We have seen 16 such cases in the past 3 years although only 3 of these were receiving the drug because of epilepsy. The patient develops inco-ordination, a staggering gait, and thick speech. This may advance to frank delirium with hyperactivity, delusions, hallucinations, and even coma. One of our patients who was treating himself with a mail order epilepsy nostrum was committed to mental institution before the condition was recognized. The psychosis is related to the concentration of bromide in the blood and tissues, and the well known bromide skin eruption is usually absent. The blood bromide is almost invariably above 150 mg. per cent. Treatment consists in replacing the bromide by some other drug, and by giving 12 to 15 g. of sodium chloride per day. The chloride replaces the bromide ion and the psychosis

clears quite rapidly. Despite these disadvantages there is an occasional case of epilepsy in which the bromide give better control of seizures than any of the other drugs.

Phenobarbital is probably a more effective drug and certainly causes fewer toxic manifestations. Moderate doses may not cause dullness; larger doses, however, may be necessary to control seizures and unfortunate slowing of cerebrations results. The addition of small doses of benzedrine sulphate or of caffeine may abolish the mental dullness without altering the anticonvulsive effect of the phenobarbital. A total of  $1\frac{1}{2}$  to 2 grains of phenobarbital per day, divided into several doses, may suffice to control seizures, but we have sometimes been forced to raise the dose to 9 grains daily before the seizures were controlled or the drug was abandoned. Phenobarbital is also available in soluble form for use in prescriptions. This sodium salt contains 10 per cent. less phenobarbital than the phenobarbital itself. Liquid preparations should not be kept for more than 3 weeks, since absorbed CO tends to precipitate the acid form of the drug.

Phenobarbital soluble is valuable when given intravenously or subcutaneously in doses of 1 to 5 grains for the control of status epilepticus. In this emergency however we prefer to use avertin administered by rectum in  $\frac{2}{3}$  the usual anaesthetic dose.

Dilantin (sodium 5,5-diphenylhydantoinate), a new drug, has already proved its merit, and has practically remade the lives of some epileptic patients. It has high anticonvulsive power and has the great advantage of causing no hypnotic effects or mental dulling. Occasionally it has mild stimulating effects. We have seen patients who were apathetic, querulous, and inclined to temper outbursts transformed into pleasant, agreeable and brighter people when sedative drugs were replaced by dilantin.

In a large series of cases dilantin has proved more effective in stopping or lessening seizures than either phenobarbital or bromides. It is especially effective in controlling psychomotor seizures, the so-called psychic variants, or states of motor automatism which are little influenced by the bromides or phenobarbital. Like other drugs, dilantin is much less effective in controlling petit mal attacks. It may indeed aggravate them. In the end, persistent and conscientious trial is necessary to determine which drug is the best for the individual patient. We have one patient whose seizures have been completely abolished with dilantin, whereas a cousin's attacks were made worse with it but are well controlled with phenobarbital.

Dilantin is analogous to the barbiturates, but is a derivative of glycolyl urea instead of malonyl urea. It is only soluble in alkaline solution, and therefore cannot be given intravenously. The drug is available in capsules containing  $1\frac{1}{2}$  grains for adults and  $\frac{1}{2}$  grain for children. The usual dosage for adults is  $1\frac{1}{2}$  grains three or four times daily, although we have exceeded that amount on occasion.

A tendency to gastric distress can be avoided if the drug is taken during the course of a meal or with milk before retiring. The dosage is proportionately less for children, and the powder may be mixed with cream if they are unable to swallow capsules.

If adequate doses of dilantin fail to control attacks the addition of small doses of phenobarbital sometimes meet with success. The most suitable combination is a matter for clinical trial.

Certain mild toxic phenomena are quite common with dilantin. After a few days of full dosage there may appear some degree of nystagmus, diplopia or difficulty in focusing the eyes, and moderate dilatation of the pupils. There may be dizziness, inco-ordination of the limbs, and staggering gait. These symptoms sometimes pass off in a few days or it may be necessary to reduce the dose for a week. Resumption of the full dose may then not lead to a return of toxic symptoms. Only rarely is it necessary to discontinue the drug.

Quite exceptionally a patient appears to be sensitive to dilantin and reacts with sharp fever, sore throat, or a skin rash. The latter is a red, macular eruption involving the trunk and limbs, and may be intensely itchy. It may appear within a day or so of commencement of the drug or after as long as three weeks. Hirsutism, swelling of the face and psychotic manifestations have been described in individual cases.

A much commoner but not very troublesome complication is a curious hyperplasia of the gums, occasionally with soreness and some bleeding. Kimball noted this change in over 50 per cent. of his cases, but the incidence is certainly much lower. He attributed it to a vitamin C deficiency, but this view has not been confirmed by others. With good oral hygiene the condition has not forced us to discontinue the drug in any of our cases.

It is felt that toxic side effects are less apt to appear if the dosage of the drug is worked up gradually over the course of several weeks to the desired maintenance level. If one wishes to change a patient over from phenobarbital to dilantin, the replacement should be made gradual.

A satisfactory method is as follows: If a patient is receiving phenobarbital 3 times daily only one of these doses should be replaced by a dose of dilantin to begin with. After three days further replacement of one dose can be made, and so on every three days until the patient is receiving dilantin alone 3 or 4 times daily. This method reduces the danger of releasing seizures through sudden withdrawal of the phenobarbital.

The use of dilantin requires careful supervision by a physician and intelligent manipulation of dosage. It will then be found to work like a miracle for some patients, to benefit quite a number of others, and in a few instances to be useless.

Mebaral (methylethylphenylbarbituric acid) is a drug with which we have not had wide experience. In a small series of

14 cases, 8 (57 per cent.) were benefited. Reports from elsewhere indicate that it may be very satisfactory in some cases which are not controlled by other drugs. It is relatively free of toxic and hypnotic qualities and deserves wider trial. The usual dosage is 3 grains, two or three times daily.

Success with any of the above named drugs often requires painstaking trial and adjustment of dosage. Too often the physician looks upon the situation with gloomy pessimism, writes a prescription for phenobarbital, and washes his hands of the matter. It is important also to individualize treatment. Some patients have their attacks only at night, and should thus receive a larger proportion of their medication before retiring. Some women have attacks only at the time of the menstrual period, and should obviously be given greater protection at that time.

The above discussion has dealt with but a few of the many questions that arise in the care of the epileptic patient. Others include the use of ketogenic diets in children; the question of rest and exercise and proper elimination; the avoidance of dangerous occupations; the problem of marriage, of bolstering the patient's morale, of tempering the family's shame and humiliation, of advising upon inheritance of a condition which may be many different conditions aping one another.

Idiopathic epilepsy should be a hopeful condition. It can be diagnosed early before there is mental deterioration, and we find no structural impairment of the brain as in many other diseases. Education will remove the stigma from it as from cancer and tuberculosis, which until recent years were cloaked with ignorant shame. Investigation and research will some day reveal the physico-chemical mechanism which allows such seizures to occur.

(The "Canadian Medical Association Journal," August 1941.)

### THIRD BOMBAY PROVINCIAL CONFERENCE OF THE ALL-INDIA MEDICAL LICENTIATES' ASSOCIATION, AHMEDABAD.

SUNDAY 21st DECEMBER, 1941.

PRESIDENTIAL ADDRESS

BY DR. U. B. NARAYANARAO.

Dr. Mehta, Brother and Sister delegates, Ladies and Gentleman,  
Presidential Addresses of our Conferences in the past have been a chronicle of all the important events concerning the Association that happened in the previous years, wherein was presented a

balance sheet of the successes and failures as well as a programme for the coming year. Most of these problems have already been so ably dealt with in the welcome address of the Chairman of the Reception Committee and the inauguration speech of our esteemed colleague that any repetition will be superfluous. Medical India, like political India, realising fully well that the cancer of communalism has been the main stumbling block in its progress—moral and material, social and intellectual,—has come to the conclusion that its salvation lies in the concentration of all its energies and efforts in eradicating this root cause of all the existing evils. I would therefore crave your indulgence to deviate from the usual convention of tackling the many problems confronting us and deal with only one subject which I believe to be of outstanding and immediate importance to us; viz. the standardisation of the medical education of our country by the abolition of the existing compartmentalism in the profession. Once we have achieved this objective, I am confident that all the other disabilities will take care of themselves or could be easily remedied.

I have to offer my sincere thanks and gratefulness to the members of the various branches of the Association in the Presidency, representing the four thousand and odd licentiates—for having elected me to guide the deliberations of this Conference.

#### OUR ELDERS.

It is a matter of supreme satisfaction and pleasure to have amongst us this afternoon, one towering personality—one who has dedicated the best part of his life to the service of the licentiate class, one who is the only surviving founder-member of our great organisation, but who, in his able but unostentatious way has been guiding us all in our forward march—I refer to our most respected and venerable Jamiatram Dada. Our eyes also turn to another equally great personage—small in stature but giantly in spirit of selfless work—I mean our revered Benjamin Dada. Brother and sister delegates, it is left to us the younger generation to continue the work along the path they have chalked out for us till the goal is reached. Let us all pray to Almighty to spare them for many more years to come to guide us and to see and enjoy the fruits of their life long labours.

#### THE GLORIOUS PAST—AND THE PRESENT ROT.

Friends, our goal has been decided once for all. But it is not without a heavy heart that this century and a quarter old class resolved for self effacement, as its final goal. In the usual course of evolution, a class which was mainly responsible for catering to the requirements of the Government and the nation, one which was rightly termed as the bulwark of the profession, in short a class with such a glorious past should have been a source of pride to any Government, should have been a tower of strength to any country. But in our unfortunate land, that was not to be. Ever since the

seeds of the compartmentalism in the medical education were sown, with the establishment of the Universities in 1858, the licentiates began to feel the effects of this invidious distinction. All these years, especially so, after our parent organisation was founded in 1906, when most of the members were in service, the licentiates utilised all their energies, all their resources in all possible ways to stop the rot. They appealed to the authorities for improvement in their pay and prospects consistent with their position in life but excepting a few concessions here, a few crumbs there, their appeal was in vain. Their cry for scope for higher studies and recognition by the General Medical Council was not heard. Their pleadings for betterment of their status fell on deaf-ears. Their petitions were unheeded and the protests received scant respect. With the increase in the output of University men, Government services were being gradually blocked to them. Graduates were taken up even in their cadre. The local bodies and even private managed institutions followed suit. Yet the class was being manufactured and the licentiates had to establish themselves in private practice in larger and larger numbers with successful careers. A systematic propaganda was then started by vested interests against the class, of unhealthy competition. Whether in the services of Government or States, Local Boards, or Municipalities, whether in the Indian Medical Council or Provincial Councils, the teaching institutions, and in private practice, humiliating treatment was meted out to them. Even most of the congress Governments have them a cold shoulder and treated them in a stepmotherly fashion. Parcelled and crushed at every step in all walks of life, the licentiates decided that the permanent abolition of the class was the only honorable solution to their ever increasing troubles. This selflessness at last opened the eyes of the Government and the other sections in the profession. Madras was the first province to abolish the class. U. P. recently followed suit. The Bombay Government have also been planning for the abolition of the Medical Schools. We understand that arrangements have been complete for a five storied building in Ahmedabad for the housing of the Hospital and the contemplated medical college. Due to want of supply of building materials the scheme had to be postponed till after the war. In Poona the Government seems to have decided to admit undergraduates for the prosecution of M. B. B. S. studies from 1943. The Hyderabad School will be looked after by the Sind Government. The other two viz. The National Medical College and Miraj Medical School shall have to come up to the University standard or close down.

#### COLLEGE OF PHYSICIANS AND SURGEONS—A HUGE FAILURE.

The tragic confusion of the dual system of medical education in the country has been worse confounded by the triple control in our presidency—the University, the Government and the College of Physicians and surgeons, the latter two, looking after the medical

schools. This college was started in 1913 with a high ideal to be an institution, similar to that of the Royal Colleges of England. But the actual constitution and working of the College has proved to the hilt that it has failed miserably in achieving this noble ideal. The licentiates, its own alumni, were not given any voice in the affairs of the college. It placed unnecessarily severe restrictions for those aspiring for its membership and fellowship. To-day a licentiate can obtain the M.B.B.S. degree in  $2\frac{1}{2}$  years, but he will require 3 years for obtaining the much inferior diploma of M.C.P.S. of the College. An instance of object irresponsibility running riot. Hon'y. fellowships till recently were the monopoly of the graduates. The rules, revised lately, are such that no self respecting licentiate would ever care to go in for the fellowship. The College does not consult or respect the views of the organised medical profession of the country in matter medical. It has not yet obtained recognition of the Indian Medical Council for the M.C.P.S. and not even the F.C.P.S. by examination. The proceedings of this so called public institution is a closely guarded secret, and not available to the class.

#### INCREASED COURSE AND MANGALDAS STATEMENT.

As if to crown all these inglorious acts of commission and omission, the College has from last June onwards increased the course of the licentiates to  $4\frac{1}{2}$  years—just six months shorter than that of the University, thus creating a further division in the class; and this, at a time, when even the Government are contemplating to abolish the class. The College Council consists of 24 members (elected from amongst 100 Fellows), some of whom happen to be the front rank leaders of the Indian Medical Association, and it is a thousand pities that these members have fallen in line with the views of the diehard elements in the Council, thus openly going against the sacred resolutions of that Association. The college authorities have added insult to injury by trying to justify this action by saying that the Licentiates themselves have been asking for this reform and that it is in the interest of the profession. There cannot be a greater perversion of facts than this. Let me therefore publicly refute the Mangaldas statement on the subject, that recently appeared in the press, and repeat that the Licentiates have been asking for a full five years course which will conform to the standard laid down by the Indian Medical Council and nothing less than that. Let me reiterate our demand for the abolition of all the existing medical schools and examining bodies and replace them by Colleges affiliated to the Universities.

#### M. C. P. S. SNARE.

A suggestion has recently been made in interested quarters that the new course should be accepted but the students passing through should be given the M.C.P.S. diploma of the College.

We know the value of this diploma too well to be lured away by these lip-sympathisers of our aspirations. The bitter

experience of Madras where the D.M.S. was given to the L.M.P. students who put in a five year course in the medical school there, should prove to be an eye opener to us that these diplomas will only mean further differentiations in the class. Let us not be a party to this game. Let us oppose this move tooth and nail. As I said recently in another platform, D.M.S. of Madras has been a delusion to the Madras Subassistant surgeon, and this much boosted M.C.P.S. is going to be, if anything, a Magna Carta of Perpetuation of Sectarianism amongst the licentiates.

#### THE COLLEGE SHOULD GO — OR ?

Friends, the past history of the College regarding the Licentiates education reveals a sorrowful state of affairs. It has treated its own alumni with such callous indifference that the Licentiates—who ought to have been proud of the Institution—are today ashamed to own it as their *Alma Mater*. It is high time that the College dissolves itself or is abolished. It has outlived its existence. The autocratic and reactionary body should go; and if even the dying pangs of the wounded heart of the Licentiates are not to move the authorities, the only next course left to us will be *Direct action*—and this the Conference will have to seriously consider. But let us hope—hope against hope—that wiser counsels will still prevail and both the Government and the College would join together and abolish the class altogether.

#### URBAN AND RURAL MEDICAL PROBLEMS.

There has been an argument that if the medical schools are closed and the starting of the Colleges unavoidably delayed for a couple of years, the medical needs of the country will suffer. It should be noted in this connection that we are apt to forget the large number of indigenous practitioners who have been rendering useful service to the public mostly in rural areas. The twenty one millions of the people of our presidency are looked after by about 10,000 allopathic practitioners and about 15,000 registered under the new 1938 Act. This proportion of one medical man to every 800 of the population does compare very favourably with that of the other countries. No doubt there is congestion in urban areas but the turning out of about 80 to 90 Licentiates per year is not going to solve the problem of rural medical needs, because there is no likelihood of their ever going to these places, the fulminations of Cursetjis and Chokseys notwithstanding. Persons who talk tall about our duties to the public, who lecture and preach us lessons on self sacrifice usually forget that we have also stomach in our bodies, that we are to look to the needs of our families and dependants first, and that charity should always begin at home. People who take pleasure in dinning to our ears in season and out of season the 'go-to-the villages slogan' know little of the village priest *cum* physician *cum* philosopher who practically holds the lives of the peoples of the village

in his palm. It has been virtually his hereditary right for generations and the people under his domain have blind faith in him. To successfully compete with such persons and to oust them from influencing the ignorant and the gullible public will be no mean task either for the ill qualified or the well qualified medical man. This is a serious problem which requires the combined efforts of the state, the public and the profession.

At this juncture one point I would like to stress that the erstwhile divisions in the profession has caused untold miseries, and the fight for freedom and rights of one class as against the other,—of licentiates vs. graduates,—has completely wasted the energies of both the contending parties. It is time that the profession realises this important fact and tries to end these troubles once for all.

#### ONE RESOLUTION.

Friends, the burden of my theme is finished. It remains for me to suggest that at this critical moment of the history of our Association, we should terminate the deliberations of our conference by passing only one resolution on this subject. That will prove to the powers—that be our earnestness, seriousness and determination to win our freedom at all costs. That will have an immense propaganda value in focussing public opinion on our just and fair demands; that will, I believe, have an effect more than that of all our resolutions of all the past years combined together.

#### WORLD WAR—OUR BATTLE.

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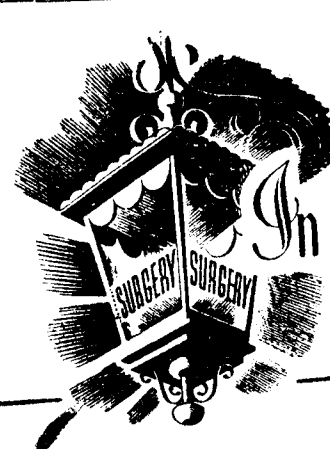
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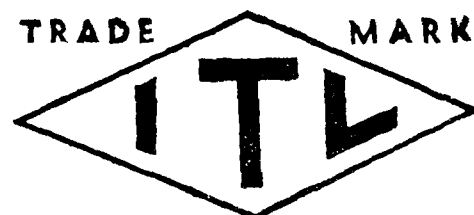
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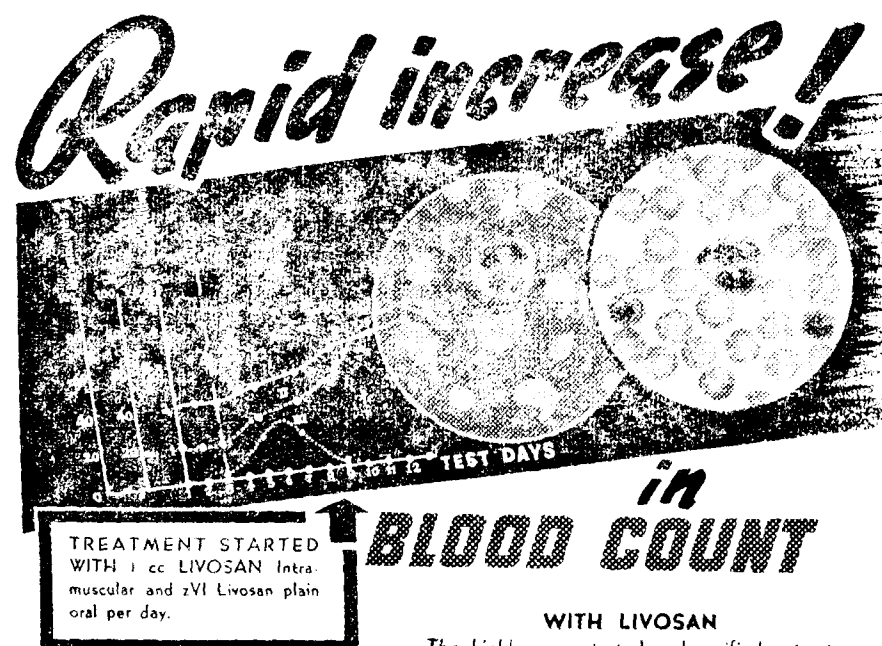
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### THE CAUSES AND PREVENTION OF BLOOD TRANSFUSION REACTIONS.

LEO M. ZIMMERMAN, M.D., ANNE MARIE STRAUSS, M.D.  
AND HAROLD LAUFMAN, M.D.

Chicago.

The last few years have witnessed a tremendous increase in the therapeutic use of blood transfusion. At the Michael Reese Hospital, for example the number of transfusions given increased four-fold in the past five years, from an already high figure of 500 per annum in 1936 to approximately 2,000 in 1940. This broadening in the application of blood transfusion has co-incided largely with the general acceptance of the indirect method. When the citrated blood transfusion was introduced by Lewisohn in 1915, it was not generally adopted because of the belief that citration impaired the value of the transfused blood and, more importantly, because of the fear of the chill reactions. These reactions were thought to be inherent in the citrate method. The intervening years have failed to disclose any striking impairment in the therapeutic value of blood by citration. Recently, it has been convincingly shown that citrate transfusions need carry no higher incidence of febrile reactions than do the direct methods, and that such reactions can be largely avoided by scrupulous cleanliness in the preparation of solutions and equipment. As a result, there has been a rapid and universal swing toward the citrate method of transfusion. Growing out from citrate transfusions have come the blood banks, plasma and serum transfusions, and other innovations that have further augmented the popularity of transfusion therapy.

The facility with which modern transfusions are done, and their very wide employment, carry with them a challenge that we control the incidence of untoward reactions. The purpose of this paper is to describe the evolution of the Blood Transfusion Department of the Michael Reese Hospital, and to trace the gradual diminution in the incidence of post-transfusion reactions.

For a number of years prior to 1937, the Strauss modification of the Lindeman method of transfusion was used routinely in the Hospital. This method employs multiple large syringes which are

alternately filled from a cannula in the vein of the donor and immediately emptied into the vein of the recipient. The syringes are successively rinsed in water, saline and citrate solutions. This study of the incidence of blood transfusion reactions was begun during the time that the above method was being used, with an analysis of the incidence of reactions in a series of 500 consecutive transfusions given during the year 1936.

When the citrate method was re-introduced into the Hospital, there was, almost overnight, a complete turn from the direct to the indirect method. The first citrate transfusions were done by essentially the original Lewisohn technique. The blood was drawn from the donor into a beaker or flask containing citrate solution, and carried to the patient's room, where it was infused by gravity, using several thicknesses of gauze to filter out small clots. As was to be expected, reactions occurred which called for the development of better methods. A second series of 500 consecutive transfusions drawn from this period was analysed for comparison of the incidence of reactions.

To improve the results of blood transfusions, a new transfusion department was organized. It was apparent from the start that there were numerous potential sources of error and disaster in the multiplicity of preliminary steps associated with the operation of blood transfusion. The first requirement, therefore, seemed to be the centralization of all of the component steps of the procedure into one department, under the sole and unified responsibility of a single administrator. Obviously, if the typings and compatibilities were done by one group, the solutions made up by another and sterilized by a third, the equipment cleansed and assembled by still another *et cetera*, it would be impossible to place responsibility or to determine the source of reactions, if they did occur.

The second requirement seemed to be special quarters and personnel allotted exclusively to this important work. Bleeding rooms were provided for the sole purpose of drawing blood for transfusions, and space was set aside for the cleansing and assembling of the apparatus. Fulltime technicians and their assistants were assigned to carry out these functions. In this transfusion center, all of the phases of the operation, from the washing of the tubing to the bleeding of the donor, were done. To obviate errors in compatibility, well-trained technicians were made available 24 hours a day. Blood groupings were done, of course, on all recipients and prospective donors, and reciprocal cross-agglutinations of cells and sera of both patient and donor. Only high titer testing sera were used for typing, to prevent errors from the presence of weak agglutinins.

In order to reduce the possibilities of contamination with foreign protein material, which might be capable of giving rise to pyrogenic

reactions, commercially prepared vacuum flasks containing citrate solution were adopted. These flasks are sealed and sterile, and are free from pyrogenic contaminants. The technic of their use is very simple. Blood is drawn by vacuum through a short length of rubber tubing from the cubital vein of the donor, into the closed flask. When the needle is withdrawn from the stopper, a sealed, sterile bottle of citrated blood is available for immediate infusion, storage, or conversion into serum or plasma, as may be desired. Injection of the blood is done by gravity through an infusion set which is equipped with a drip-chamber and a fine-gauge metal filter to remove minute clots.

The Transfusion Department was made responsible for the maintenance of adequate active lists of professional donors. Rigid requirements were established for persons desiring to give blood for transfusion. Only healthy young males with good veins are selected. A careful history is taken of each candidate to rule out allergy, tuberculosis, malaria and syphilis. Record is made of previous infections from which the donor has recovered, for use when immune transfusions may be desired. A complete physical examination is done, including Wassermann and Khan tests, complete blood counts, and differential blood smears. No professional donor is used oftener than once in six weeks, and the serological tests are repeated every six weeks. In addition, the genitalia and the oral cavity are inspected immediately before blood is drawn for transfusion, in order to rule out recent syphilitic infection. Donors must remain on call, and be within 20 minutes reach of the hospital. It is thus possible to deliver blood to the patient within 30 minutes from the time the call is received in the transfusion center.

When friends or family-members wish to act as donors, such careful selection cannot be made. Nevertheless, in addition to the typing and compatibility determinations, an immediate Khan test is done and, if possible, the genitalia and oral cavity are inspected for evidences of early syphilis.

Special attention is given to the problem of cleansing and assembling transfusion apparatus. As has been stated, full-time employees carry out these tasks in space set aside for the purpose. Metal and glass parts are thoroughly washed in acid solution and distilled water. Rubber tubing is boiled, first in weak sodium-hydroxide solution, then in distilled water.

In order to be sure that no pyrogenic foreign material remains in the equipment, a sample of the final washings are subjected to a "pyrogen test." This consists of injecting such fluid into the veins of rabbits. If protein contaminants are present, the animal exhibits a typical chill and fever reaction, identical with that seen in human beings. This constitutes an accurate biological check on the safety of the equipment.

A system of checks and double-checks has been developed to prevent erroneous labelling of the blood samples when several transfusions are being prepared at the same time, and to prevent injecting the blood into the wrong patient. Furthermore, a careful follow-up has been instituted to record the post-transfusion course. This not only permits an accurate determination of the incidence, type and severity of reactions, but also makes it possible to check back and trace the source so that it may be eliminated.

#### BLOOD TRANSFUSION REACTIONS.

We have classified our reactions under three headings, the pyrogenic, allergic and hemolytic. Pyrogenic reactions constitute far the greatest number of post-transfusion disturbances. They consist of a sharp elevation of temperature, coming on during or shortly after a transfusion, with or without an accompanying chill. If the maximal temperature elevation exceeds two degrees, it is classed as a major reaction, otherwise it is considered to be minor. These chill and fever reactions are not, of themselves, dangerous. However, the added load they may impose upon patients already critically ill cannot be disregarded.

It has been convincingly shown that chill reactions are almost invariably due to the inadvertent injection of foreign protein material into the blood-stream. The source of protein contamination may be bits of old blood left in the tubing or needles, powder from the tubing, or pyrogenic material incompletely removed from the water during the process of distillation. The potential sources are, therefore, legion, and only by scrupulous care and everlasting vigilance can such reactions be averted. When they do occur, prompt revision of the entire process, with repetition of the pyrogen test, is in order, so that the source of error may be detected and eliminated.

Allergic reactions are rarely serious. They usually manifest themselves by urticaria, less frequently by asthma or other visceral disturbances. Such reactions have been known to occur following repeated transfusions from the same donor, or from donors with definite allergic tendencies. Blood drawn soon after the donor has eaten may also give allergic reactions. Allergic persons, therefore, should not be used as blood donors and, whenever possible, blood should be drawn during the fasting state.

Hemolytic reactions are always serious, and may be fatal. They are due, as a rule, to the transfusion of incompatible blood. Fortunately, with the use of careful typings and compatibility tests, such reactions are extremely uncommon. *No such reactions have occurred in the entire series of transfusions here reported, nor have any been seen during the entire duration of the Transfusion Department.* The clinical manifestations of hemolytic reactions are severe lumbar pain, dyspnea, chills, varying degrees of collapse, vomiting, followed by jaundice and hemoglobinuria. These may lead to oliguria or

anuria, and death from uremia may ensue. The prevention of this type of reaction demands utmost care in the performance of the typing and compatibility tests. Emphasis is placed upon the use of only high-titer testing sera. All questionable bloods should be rejected. Cross-typings of both cells and serum of donor and patient should be done. These precautions will obviate the danger of sub-group agglutinations and, as will be shown later, will permit the safe use of universal donors.

*Incidence of Reactions.* In order to determine the actual incidence of blood transfusion reactions, and to compare this incidence with successive modifications in the technique of transfusion, we have studied five series of 500 transfusions each. As has been stated, the first series was drawn from the period in which the direct method was being used, and the second from the period of "open" citrate transfusions. A third sample of 500 cases represents the early experience in the new transfusion center. A fourth series was taken during the second year of the activities of the center, and a final 500 recent transfusions represent our present incidence of reactions.

The results of this study are seen in Table I. It will be noted that the direct method gave a rather high incidence of reactions

TABLE I.  
INCIDENCE OF REACTIONS FOLLOWING TRANSFUSIONS.

|                                                                         | Major.        | Pyrogenic<br>Reactions<br>Minor. | Total.        | Allergic<br>Reactions. | Hemolytic<br>Reactions. | Total<br>Reactions. |
|-------------------------------------------------------------------------|---------------|----------------------------------|---------------|------------------------|-------------------------|---------------------|
| <b>Series I</b>                                                         |               |                                  |               |                        |                         |                     |
| 500 Consecutive<br>Direct Transfusions<br>(multiple syringe)<br>1936    | 25<br>(5.0 %) | 14<br>(2.8 %)                    | 39<br>(7.8 %) | 9<br>(1.8 %)           | 0                       | 48<br>(9.6 %)       |
| <b>Series II</b>                                                        |               |                                  |               |                        |                         |                     |
| 500 Consecutive<br>Indirect Transfusions<br>(open method)<br>1938       | 30<br>(6.0 %) | 5<br>(1.0 %)                     | 35<br>(7.0 %) | 2<br>(0.4 %)           | 0                       | 37<br>(7.4 %)       |
| <b>Series III</b>                                                       |               |                                  |               |                        |                         |                     |
| 500 Consecutive<br>Indirect Transfusions<br>(Early New Method)<br>1939  | 19<br>(3.8 %) | 7<br>(1.4 %)                     | 26<br>(5.2 %) | 10<br>(2.0 %)          | 0                       | 36<br>(7.2 %)       |
| <b>Series IV</b>                                                        |               |                                  |               |                        |                         |                     |
| 500 Consecutive<br>Indirect Transfusions<br>(Recent New Method)<br>1940 | 8<br>(1.6 %)  | 6<br>(1.2 %)                     | 14<br>(2.8 %) | 5<br>(1.0 %)           | 0                       | 19<br>(3.8 %)       |
| <b>Series V</b>                                                         |               |                                  |               |                        |                         |                     |
| 500 Consecutive<br>Indirect Transfusions<br>Feb. to May, 1941.          | 3<br>(0.6 %)  | 8<br>(1.6 %)                     | 11<br>(2.2 %) | 4<br>(0.8 %)           | 0                       | 15<br>(3.0 %)       |

(9.6 per cent.), chiefly of the pyrogenic type. This, in retrospect, is not surprising in view of the fact that the importance of removing pyrogens from equipment and solutions was not appreciated. It is a tribute to the method, which permitted but little contact of blood with foreign surfaces, that reactions were not more numerous. The first citrate transfusions showed, surprisingly, a slightly lowered incidence of reactions (7.4 per cent.). The multiple potential sources for these mishaps has been mentioned. Nevertheless, there was probably less contact with impure solutions, resulting in the lowered incidence of febrile reactions.

The first 500 transfusions under the present set-up (Group III) were somewhat disappointing. Although there was some reduction in the number of reactions, this was not as striking as had been anticipated. However, adequate records and the use of the pyrogen test permitted a progressive elimination of the various responsible factors. This is reflected in the fourth series, in which the total incidence of reactions was 3.8 per cent., and the major febrile reactions had been reduced to 1.6 per cent. The last series of 500 recent consecutive cases shows a total incidence of slightly over 2 per cent. reactions, and only 0.6 per cent. major pyrogenic reactions. This very creditable figure proves the possibility of reducing transfusion hazards to a minimal figure. With continued alertness and further improvement in technique, there is every reason to expect still more reduction in transfusion reactions.

Further analysis of a series of 1,000 consecutive transfusions to determine the relationship between the frequency of reactions and the disease state for which transfusion was done indicates that certain pathological conditions predispose to the various types of reaction. (Table II) Thus, blood dyscrasias gave a much higher frequency of pyrogenic reactions than did other disease, while ulcerative colitis gave an excessive number of allergic reactions. Septic states, generally, seemed to predispose to febrile reactions suggesting that these persons are sensitive to minute and otherwise innocuous quantities of pyrogenic material. Chill reactions in those patients could be prevented by giving multiple small transfusions, none exceeding 250 cc. of blood.

The incidence of reactions following transfusion of blood from universal donors, as compared with blood from donors of the same blood group as the patients, is revealed in Table III. It will be seen that the incidence is actually lower in the former group. We believe, therefore, that it is safe to administer universal donor blood to patients of other blood groups provided, by the use of high-titer testing sera, the correct type of the donor's blood is assured. Careful direct compatibility tests between recipient and donor bloods must be made to rule out anti-o agglutinins in the patient's serum.

TABLE II.  
THE INCIDENCE OF TRANSFUSION REACTIONS IN PATIENTS  
CLASSIFIED ACCORDING TO DIAGNOSIS AND DEPARTMENT.

|                    | No. of Transfusions.        | Pyogenic Reactions. | %  | Allergic Reactions. | %  | Total Reactions. | %    |
|--------------------|-----------------------------|---------------------|----|---------------------|----|------------------|------|
| Medical Patients.  | Gyne. Surgery.              | 56                  | 4  | 7.1                 | 1  | 1.8              | 8.9  |
|                    | Orthoped. Surgery.          | 29                  | 0  | 0.0                 | —  | 0                | 0.0  |
|                    | All other Surg. Depts.      | 415                 | 10 | 2.4                 | 3  | 0.7              | 3.1  |
|                    | Blood Dyscrasias.           | 45                  | 8  | 17.7                | —  | 8                | 17.7 |
| Surgical Patients. | Ulcerative Colitis.         | 50                  | 1  | 2.0                 | 5  | 10.0             | 12.0 |
|                    | All other Medical Diseases. | 340                 | 13 | 3.8                 | 5  | 1.4              | 5.2  |
|                    | Obstetrics.                 | 65                  | 4  | 6.1                 | 1  | 1.5              | 7.6  |
|                    | Totals.                     | 1,000               | 40 | 4.0                 | 15 | 1.5              | 5.5  |

TABLE III.  
INCIDENCE OF REACTIONS IN PATIENTS TRANSFUSED WITH BLOOD  
OF THE SAME TYPE AND IN THOSE RECEIVING BLOOD OF A  
DIFFERENT TYPE (UNIVERSAL DONOR BLOOD)

|                                               | Number of Transfusions. | Pyogenic Reactions. | Allergic Reactions. | Total Reactions. |
|-----------------------------------------------|-------------------------|---------------------|---------------------|------------------|
| Patients and Donors of Same Blood Group.      | 780                     | 35 (4.5%)           | 12 (1.5%)           | 47 (6.0%)        |
| Patients and Donors of Different Blood Group. | 220                     | 5 (2.2%)            | 3 (1.4%)            | 8 (3.6%)         |
| Total.                                        | 1,000                   | 40 (4.0%)           | 15 (1.5%)           | 55 (5.5%)        |

#### SUMMARY

1. The control of blood transfusion reactions demands centralization of responsibility over all of the component steps of the operation, careful supervision of the numerous potential sources of error, and everlasting alertness to trace to eliminate factors causing untoward reactions.
2. The organization of a Blood Transfusion Department for a general hospital is described.

3. Five series of 500 transfusions each are analysed, tracing the gradual elimination of the causes of reaction with corresponding improvement in the results.
4. The pyrogen test is an effective aid in controlling the preparation of solutions and equipment.
5. Reactions following transfusion are classified as pyrogenic, allergic and hemolytic.
6. Pyrogenic reactions, characterized by chills and fever, are most frequent. They are almost invariably due to the presence of foreign contaminants in the solutions or apparatus. Sepsis and blood dyscrasias predispose to pyrogenic reactions.
7. Allergic reactions are usually urticarial in nature. The chief causes are donors with allergic tendencies and blood taken shortly after the donor has eaten. Patients with ulcerative colitis seemed to be predisposed to allergic reactions.
8. Hemolytic reactions are due to the infusion of incompatible blood. This can be avoided only by careful preliminary typings and reciprocal cross-matchings, the use of high-titer testing sera, and the rejection of all bloods giving questionable agglutinations. There were no hemolytic reactions in our series.
9. Universal donor blood gave no higher incidence of reactions than did blood of homologous groups.
10. Our statistics reveal reduction in the reaction incidence from 9.6 per cent to 2.2 per cent. Only 0.6 per cent of the latter figure were major pyrogenic reactions. Our experiences point the way to further reduction in the incidence of transfusion reactions.

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## THE PHYSIOLOGICAL CHANGES INCIDENT TO PUBERTY

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A review of the information available at present on the subject of puberty shows our knowledge to be quite ample on many insignificant points, and very meager on some of the most important ones. Thus the appearance of pubic hair in boys is certainly one of the less significant changes of puberty, but it is one of the easiest to study and so has furnished some of the most quantitative information we have. The appearance of the ability to reproduce, on the other hand, is the most essential phenomenon in adolescence, and is properly emphasized as such in dictionary definitions of puberty; but in the nature of things it is all but impossible to determine this

ability directly either in the individual case or in groups for statistical purposes. Thus we have the least knowledge of this most important aspect of puberty.

If we agree that a knowledge of the normal is indispensable for the diagnosis of the abnormal, then we must deprecate the absence of accounts of normal puberty in textbooks of physiology, gynecology, and urology. The writer has before him four books on these subjects; although they vary in length from 700 to 1200 pages, they do not contain the word "puberty" in their indexes.

Hope of increasing our knowledge of this subject is offered by various investigative methods, among which statistical method at present appears especially promising. To illustrate this point is one of the purposes of this paper; another purpose is to offer a summary of the pubertal changes in the normal boy and girl.

*Growth Curves in General*—Harris, Jackson, Paterson, and Scammon found that the organs and parts of the body could be classified into four main categories according to the forms of their growth curves. In each category the period of life from 12 to 16 years shows something characteristic.

Organs and parts of the "general type," such as the bones, muscles, lungs, and kidneys, experience a marked acceleration of growth during this period. Because these organs outweigh the other parts of the body, the weight and dimensions of the body as a whole show the same marked acceleration. The individual person shows the acceleration even more markedly than does the average for a group of people.

Organs of the "neural type," such as the spinal cord, differ from the above in that they participate little, if any, in the pubertal acceleration. In fact, as a result of fairly steady growth throughout childhood they reach adult weight early in puberty and remain constant thereafter. According to the measurements of Godin the brain declines a little in weight during late adolescence, having temporarily surpassed its destined adult weight at about puberty.

Organs of the "lymphoid type" are of special interest because the group includes the thymus, tonsils, adenoids, lymph nodes, and intestinal lymphatic masses. These structures reach the peak of their development just before the age of 12. At this time they are, on the average, about twice their destined adult size. This is true for the average; individual structures often far exceed this. Thereafter in general there is a rapid decline. While this fact is always recorded in connection with the thymus, as being one of the few established facts regarding that organ, its importance is not always appreciated in connection with the tonsils and adenoids.

*Genital Growth*—Organs of the "genital type" include the testicle, ovary, uterus, and so on. These organs experience a very

sharp acceleration of growth during puberty; on the average, according to the curves of Harris, et al., their weights increase ten-fold between the ages of 12 and 20. This is true for the average; for the individual organ in a particular case the rate of growth is astonishingly rapid over short intervals of time. In one case noted by Jung and Shafton the testicles must have doubled their weight (estimated on the basis of linear measurements) in six months and redoubled it in the following ten months; there was no reason to suppose this case unusual.

With the other external genitalia growing proportionately while the remaining parts of the body pursue entirely different growth curves, it is easy to see why many boys at puberty temporarily present a picture in which the genital elements may seem entirely too prominent. This has occasionally led inexperienced examiners to suspect self-stimulation as the cause. Obviously such a suspicion is based on thoroughly confused reasoning in the matter, both as regards the place of self-stimulation in the normal sexlife and as regards the way the body grows at puberty.

*Factors Determining the Onset of Puberty in Boys.*—The functions of the human body, including the growth of its various parts, are influenced by so many seasonal and geographic factors that no results obtained in a particular region at a particular time should ever be assumed uncritically to hold elsewhere and for all time. Mitoses in the human body have a diurnal rhythm; this was shown by studies on preputia removed by circumcision at various times of the day. Even the fingernails have an annual growth rhythm. The seasonal effect on the growth of children is so marked that some children even lose weight in February and March, the least favorable months. It was Crampton who showed that season has an effect on pubescence also; the duration of this period in boys is shorter if it includes summer. The seasonal and geographic influences affecting puberty in girls will be discussed below.

Part of the importance of Crampton's observation lies in the fact that an early puberty is at least temporarily advantageous to a boy. He found that if 100 boys between the ages of 14.00 and 14.99 years were sorted out by the pubic hair criterion, the averages for height, weight, strength (as measured by a dynamometer) and proficiency in school were all higher in the postpubescent group. Hence it would be of great interest to know whether there are regions, such as those of the Andes and the Rockies, where puberty might be perceptibly delayed.

Observations over a period of years or decades might also reveal a secular drift in puberty time for boys comparable to that which will be mentioned below as having been reported consistently for girls; but no data of this sort, whether geographic or secular, have yet come to the attention of the writer.

*Growth of Bone and Muscle in Boys.*—Porter and Smedley, according to Crampton, independently found a curious and striking correlation between weight and scholarship in each age group of their series of boys. Smedley found that this correlation was highest at the age of 12. Crampton found that similar correlations involved height and strength: these facts proved to have a common explanation in the fact that within each age-group the post-pubescent boys were generally taller, heavier, stronger, and scholastically more proficient than the prepubescent. If it is safe to accept the widespread belief that autoerotic activity increases markedly at puberty, one must conclude that such activity does not result in demonstrable impairment of growth, strength, or scholarship.

Crampton dispelled an old idea that growth in height and growth in weight are mutually incompatible. He also showed that the prepubertal weight-rise reported by others was a statistical illusion, present in curves for averages but absent in curves for individuals. It is not always appreciated that normal individuals must deviate in both directions from an average. Surprising spurts in weight and in height growth are seen in the individual protocols given by Jung and Shafton.

Relation of body-form to time of puberty is a difficult subject about which little can be said in boys. Of two cases of extremely late puberty in the boys seen by Jung and Shafton, one was that of an individual of rather feminine habitus, but neither subject was unusual as regarded height or weight for his age. The unsatisfactory results of attempts to classify men into leptosomic and other types do not encourage one to try to make such correlations except in dealing with widely separated racial or geographic groups.

*Skin, Hair, and Eyes in Boys.*—In an effort to see whether there was a difference in puberty time between light-haired and dark-haired boys, Jung and Shafton classified a number of boys in this way. The results at first seemed to show that dark-haired boys went through puberty on the average nearly two years before the lighter-haired boys. It was soon found, however, that this was a statistical paradox explained by some old observations of Uchida and of Pfizner. These investigators found evidence, in England and in Alsace respectively, of a deepening of hair-color and eye-color during adolescence (strongest between 16 and 19). This change is best demonstrated in statistics, but is sometimes observed in an individual case. Hamilton and Hubert also observed it in 3 out of 4 castrated men between the ages of 35 and 45 years after the administration of testosterone propionate.

Bloch found it possible to study the changes of the adolescent skin quantitatively. He found that English school boys suffered from acne most severely at the age of 18, when 57 per cent. were exhibiting it in severe form (blackheads, blotches, and pimples).

He sketched an endocrine theory to account for the increased and troublesome activity of the sebaceous glands. The condition must be described as an almost normal abnormality, since less than 1 per cent. of otherwise healthy boys escape it.

Boys poorly instructed in personal hygiene are especially likely to suffer an accumulation of smegma preputii after puberty. This may be due in part to the increased activity of the sebaceous glands already noted, in part also to the seminal emissions which should begin about this time. Modern psychology offers little justification for the old beliefs that phimosis and accumulation of smegma are important inducements to autoerotic activity, that the manipulations of stretching the prepuce and cleansing the collum glandis may initiate masturbation, or (even if all the former statements were true) that the supposedly resultant masturbation is abnormal and harmful. In view of the additional fact that the prepuce has an obvious function of protecting the glands, there is now less justification than formerly for circumcising as compared with giving hygienic instruction.

The pubic, axillary, and facial hair were found by Jung and Shafton to appear in the order named. The growth of facial hair has a certain popular interest, and the age between 16.00 and 16.99 seemed to be the critical one. Of 15 boys in that age-group, 8 had not yet shaved, 1 had shaved once, 1 had shaved twice, 1 was shaving about once a month, and 4 were shaving somewhat oftener. The appearance of hair on legs, arms, chest, and abdomen was also noted by these authors, but they were unable to make any generalizations because of the lateness and especially because of the great variability of the hair in these regions.

*Thyroid, Blood, and Gastric Acidity*—Jung and Shafton also found it impossible to reach a conclusion regarding the thyroids palpated in pubescent boys. No consistent enlargement was found. This is in contrast to the findings of Pryor in Californian girls of a significant enlargement of this gland. The difference may be either sexual or geographic.

The iron, copper, and hemoglobin in the blood of normal adolescent children have been measured by Sachs, Levine, and Griffith. Up to the 14th year the two sexes do not differ significantly. At about this age the three values for girls become constant at the levels characteristic of adult women. After the 16th year in boys, however, the values for iron and hemoglobin rise sharply; they reach the average value for adult men by the 17th year. During the 17th or 18th year the value for copper similarly reaches the value for adult men.

A similar sexual differentiation at puberty affects even the stomach. According to the statistical work of Vanzant et al. at

about the age of puberty the average value of free gastric acidity for boys begins to rise considerably above that for girls.

*The Mammary Gland in Boys*—There are no data available as to the frequency with which painful lumps under the nipples of normal pubescent boys are removed by surgeons and subsequently diagnosed as adenofibromas by pathologists, but personal communications to the author indicate that the frequency is considerable. This is simply because physiologists have not hitherto supplied a complete chronology of the growth of the male breast.

It appeared from the studies of Jung and Shafton that at least in Illinois the mammary glands of every normal boy are stimulated to renewed growth during puberty. The glandular mass (the subareolar node) is at first hard and spherical, and raises the nipple above it measurably. The nipple height thus reaches a maximum at the age of 14½ years. Tenderness is not always present, but is sometimes quite marked. About 15 per cent. of the boys are sufficiently impressed with the tenderness to remember it in later life. In the course of a few years the nodes soften and many vanish; but many older men retain palpable subareolar nodes.

In the experience of Jung and Shafton early and conspicuous subareolar nodes were correlated with apparent physical vigor, and the largest nodes seen in pubescent boys—nodes which in one case measured 6 cm. across—were in especially athletic specimens. This fact is explained by the observations of Selye and others, who obtained mammary hypertrophy in male rats after the injection of testosterone.

Since the subareolar node is a normal structure, it is misleading to refer to it as mastitis adolescentium except in the event of complications. Since it is the natural result of the action of an important hormone, one can understand why Vassal found it a very stubborn condition to treat. It also becomes unnecessary to decide between the contentions of Stumcke and Laurent on the one hand and of Franck on the other; the latter suggested autoerotic activity as the cause, the two former suggested autoerotic activity as the cure, for the subareolar node.

*Change of Voice*—The change of voice to a deeper pitch is one of the earliest and most evident change of puberty. That it can be prevented by castration is well-known. This fact is supplemented perfectly by the studies of Hamilton and Hubert on human eunuchoid subjects. For each voice the pitch of conversation and actual range was recorded before and after treatment. Testosterone propionate lowered the range and pitch. Congestion and coarseness of the membranous structures accompanied treatment and were followed by prominence of the thyroid cartilage. Withdrawal of therapy permitted partial reversion, especially in pitch.

*Genital Phenomena in Boys*—Quantitative studies on various kinds of erotic activity in boys were published by Hirschfeld. This was an important contribution, and many additional studies of the same sort in different times and places would be desirable. This is especially true because data obtained by any kind of questionnaire method are likely to reflect to some extent the prejudices of the collector.

That various erotic manifestations, including erections, are normal in boys of all ages is now generally conceded. Hirschfeld found that 15 per cent. of the boys he questioned had had sexual fantasies during or before their fifth year of life. It is generally assumed that such phenomena should increase sharply near puberty, but actual data on this point are scarce. Of 437 boys, 12 per cent. had begun to masturbate before the end of their ninth year, and more than 50 per cent. had begun before the end of their thirteenth year.

To some boys the first erotic dream with emission of semen comes as a memorable, even shocking, experience. If this were true for all, the phenomenon would be as well adapted to statistical study as is the menarche in girls; but it appears that most men do not recollect this event. After the rhythm of erotic dreams and nocturnal discharges is established it continues for years at a fairly constant level. At least two studies of this phenomenon in the adult have been published, but systematically gathered information as to its appearance at puberty and frequency immediately thereafter seems to be lacking.

No data have been found as to the time at which spermatozoa appear in the genital secretions of boys. Such data would help to give a notion as to the time at which boys become capable of generation, though it would not be conclusive. The variations found in the semen of men of proved fertility, and the facts to be mentioned below regarding adolescent sterility in girls, would render unsafe and final deductions as to fertility in boys on the basis of finding spermatozoa.

*Chronology of Pubertal Changes in Boys*:—The following summary probably gives the most usual order of the changes of puberty in boys. In individual cases the changes may occur in a different order. When a statement is made regarding an average it necessarily implies that normal individuals deviate in both directions from that average. Finally, it must also be noted that data representing some widely separated places and times cannot be applied uncritically in particular circumstances.

Year.

10. Growth of neural type of organs near by complete.
12. Maximum weight for lymphoid organs.
13. Average time for change of voice; beginning of period of rapid genital growth.

14.0. Fastest growth of pubic hair; fastest growth of body in height and weight; autoerotic activity in more than half of boys before this age.

14.5. Maximum nipple height (most frequent occurrence of subareolar node); fastest decline of lymphoid tissues.

15.0. Fastest growth of axillary hair.

16.0. Fastest genital growth (penis and testicles).

16.5. About half of boys have begun to shave.

17.0. Blood iron and hemoglobin reach adult male level.

18.0. Blood copper reaches adult male level; acne reaches worst stage.

*The Menarche* — Studies of adolescence in girls have had the advantage over comparable studies in boys in that the menarche is so definite an epoch in a girl's life. It lends itself to exact numerical treatment and has led to some convincing and informative results.

Thus, for instance, the effect of climate on the menarche has been clearly brought out by Engelmann. He found that girls of Norwegian stock living in the region of the Great Lakes menstruate about 18 months earlier in life than do girls of the same stock in Norway. In the same way it has been possible for Engle and Shelesnyak to demonstrate the effect of season. They found that the menarche is a little more likely to occur in the winter months than in the summer, and that when the menstrual cycle has already been established it is liable to slowing and irregularity when summer comes. This is in agreement with the earlier findings of Kirchhoff and the more recent ones of Breipohl.

Of equal interest is the information assembled by Mills revealing a secular drift in the time of menarche. Data obtained by a variety of investigators show that in some parts of the world the menarche has been occurring at least a year earlier than it did in the past. Such data are available from German, Dutch, and Norwegian sources; Schreiner's data from Norway, in fact, go back as far as the year 1839. Hypotheses as to the explanation are given by Howe.

*Hair-Color and Body-Build in Girls* — In addition to the environmental factors just mentioned, there must be internal, individual factors that determine the onset of the menarche. In the case of boys, the attempt of Jung and Shafton to tell whether different physical types go through puberty at different ages was found to lead to a statistical paradox. The boys had been classified as light-haired and dark-haired, and it was found that during the period of study so many boys pass from one category into the other as a result of adolescent hair-darkening that the criterion is not reliable.

Apparently the same phenomenon has been encountered in girls. Breipohl selected the 21 darkest and 179 lightest-haired out of 284 German girls, and found that the brunettes had first menstruated at

an average age of 13.02 years, while the blondes had first menstruated at 13.31. He wisely refrained from drawing a conclusion.

In the same way Pryor and Smith compared the time of menarche of the nine slenderest with the nine broadest in their series of Californian girls. While the broad-built girls had their menarches at the early average age of 11.7 years, the average could not be computed for the slender ones because when the study was terminated they had not yet all menstruated; their average was apparently destined to be well over 14. Since the same authors demonstrated a marked broadening of contour to be an essential change of puberty, it is evident that one must be careful in drawing a conclusion.

*Other Factors Affecting the Time of Menarche* Schaeffer was not able to confirm a previous report by Mayer as to a difference in time of menarche between blondes and brunettes. It is likely, however, that if more dependable criteria than hair color or skeletal measurements are used in sorting out geographic or social groups, real differences will emerge. An example is Schaeffer's finding that 1321 Christian girls averaged 14.053 years at the menarche while 480 Jewish girls averaged 13.522 years.

Schaeffer, whose observations were made in Germany, also confirmed the findings of Szukitz in Austria, Brierre de Boismont in France, and Ravn in Denmark, that girls in the country menstruated more than a year later than girls in the city. Within a given environment, also, the daughters of wealthy families menstruated about a year earlier than the daughters of laborers, and girls classified as strong menstruated earlier than mediocre or asthenic girls.

These last facts give rise to a complicated set of intercorrelations in which it becomes difficult to distinguish cause from effect. Evidently early puberty, large physical size, physical strength, good state of nutrition, superior intelligence, and favorable environment are mutually related in girls as they were seen to be in boys.

*Advantages of Early puberty in Girls.* Carter noted that the disparity between premenarcheal and postmenarcheal girls within any given age group tended to become negligible with increasing age. This is parallel to Smedley's observation in boys. In other words, the advantage of having an early puberty seems striking at first, but dwindles because the retarded individuals can be shown by actual measurement to make up for lost time. This agrees further with the conclusion of Mills and Ogle that a late menarche does not necessarily mean late appearance of fertility.

In fact, the ultimate advantage lies in having a menarche rather near the mean for the population in the given environment. This was found to be true in the study of Mills and Ogle; if the menarche occurred much earlier or much later than the average,

marriage or illegitimate first birth was delayed. Vitalli has assembled data that show that not only very late, but also very early, menarche increases the probability of the following troubles: (1) irregularity of cycle (Schroder), (2) anomalies of bleeding (Feldweg), (3) primary sterility, habitual abortion, and prematurity (Feldweg), (4) frequency of abortion (de Torres) and (5) dystocias (Weysser). Vitalli also made a remarkable quantitative study of the milk-secretion of 1386 mothers who gave the dates of their respective menarches; it was found that girls who menstruate most nearly at the average age are most likely to have satisfactory lactation. Risopoulos agrees with Vitalli that late menarche predisposes to some condition, probably narrow pelvis, of etiological importance in Caesarian operations; the data of Risopoulos were obtained in a comparison of the histories of 75 Caesarian patients with 5288 normal mothers.

*Skin and Breast*—Bloch studied quantitatively the distribution of blackheads, pimples, and blotches in girls as he did in boys. In girls these unwelcome harbingers of puberty were sometimes found as early as the age of 7, and they reached what might well be called their pessimum at the age of 17, a year earlier than that for boys.

Apparently the female breast passes through a stage comparable to that described as the subareolar node in boys, but from 3 to 5 years earlier. The youngest of the fourteen German girls in whom Zappert observed the "acute painful swelling of the breast of older children" was 8 years old; his largest group of children with this condition were 11 years old. This agrees with the finding of Pryor that the stage of the breast-bud was found most frequently in the age groups from 11.5 to 12.4 years. The subsequent development of the female breast is summarized in a table by Pryor, and the data can be checked against the illustrations in the book by Glasmer and Amersbach. The development of the breast begins before the appearance of pubic hair, and is well advanced by the time of the menarche.

*Pubic Hair*—The tabulations of Pryor include the result of classifying 74 girls at the menarche as to the stage of development of pubic hair. The largest group, 48 girls, were at that time at stage C, characterized by "terminals not over 25 mm. in length, sparse, fully pigmented, and wavy." Another table, showing the relation of pubic hair to age, indicates that a definite growth precedes the menarche by roughly a year. The axillary hair appears later than the pubic as it does in boys.

*Height and Weight Growth in Girls*—Pryor and her collaborators made a serial study of the adolescent growth spurt in 100 girls. Examinations were made at half-year intervals over a period of four years. Gain in height preceded gain in weight, and was quite evenly distributed over a period of 18 months. Pubescent girls averaged a height increase of 10.64 cm. in eighteen months compared with a

9.38 increase for non-pubescent girls of the same age. The rate of height-gain for pubescent girls during the last six months before the appearance of the menses was 26 per cent. faster than that for non-pubescent girls during the same period of time. Pubescent girls were consistently taller and broader than non-pubescent girls of similar ages in a series of 422 cases.

The same investigators also studied the weight-growth of their subjects. They found an acceleration which appeared to be specifically stimulated by the approach of catamenia. During the six months just preceding the menarche, 40 girls made an average gain of 4.2 kg. (9.2 pounds), or almost twice as much as 40 other girls of the same ages who were non-pubescent and averaged 2.47 kg. (5.4 pounds) during the same period of time. The result of this acceleration of growth is that, like boys, post-pubescent girls for a time surpass the pre-pubescent girls of their own age-group in height and weight.

*Mental Attitude in Girls.*—A remarkable illustration of the usefulness of statistical method is the discovery of Stone and Barker that they could express quantitatively so intangible a thing as the change in outlook that accompanies the menarche in girls. They used three standard tests to measure the intelligence, interest-attitudes, and developmental age of 175 postmenarcheal girls. The results were compared with others obtained by measuring a similar, homogenous group of 175 premenarcheal girls, paired for chronological age with the former group. By all three tests the post-menarcheal group was found to be significantly ahead.

*Reproductive Phenomena.*—Engle and Sholesnyak studied the first menstrual cycles of 100 girls whose medical histories and physical findings were normal. This group of girls had experienced from 20 to 69 cycles, a total of 3,140. The extreme range for length of cycle was from 7 to 256 days, with a mode at 28 days and an average of 33.9 days. Thirty-two per cent. of these cycles departed more than 14 days from the average for any given girl, and thirty-two per cent. of the cycles differed by more than 11 days from the average of the group as a whole. It is important to note that the average (roughly 34 days) differs from the most frequent figure (28 days) by as much as 6 days. The extent of normal variations revealed by this study deserves wider appreciation; it has also been emphasized by Arey.

Mills and Ogle have assembled the results of observations in man as well as of experiments with monkeys and mice which indicate that the menarche is not the same as the time when ability to conceive appears. The monkeys studied by Hartman began to menstruate when their body weights reached about 3350 grams, but did not ovulate or conceive until they reached about 5000 grams. The

mice studied by Mills and Ogle under controlled conditions of artificial climate showed a lag of about 30 days between first estrus and first conception, the duration of the lag being affected by living conditions. In the human female the corresponding lag is of the order of 5 years.

#### CONCLUSION

Our knowledge of the simple numerical facts about puberty in both sexes is still incomplete. The methods of statistical analysis in the hands of experienced workers promise to help much in giving up the data on which to base the diagnosis and treatment of abnormalities.

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### THE SCOPE OF ARTIFICIAL IMPREGNATION IN THE BARREN MARRIAGE.

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The involuntary barren marriage continues, as it has for ages, to present an important medical, economic, and psychologic problem. The oft-quoted statement that from 10 per cent to 15 per cent of marriages in the United States are involuntarily barren, while coldly accurate, does not sufficiently express the appalling degree of marital insecurity and the deep unhappiness which lie submerged in the statistics. It is, therefore, the duty of any physician consulted by a barren couple to appreciate the complexity of the situation and to bend his every effort to the solution of the difficulty. From the standpoint of the required systematic survey, it is essential that both partners be assiduously investigated for possible etiologic factor and that any possible impediment, however slight, be removed. The methods of making an organized search in each marital partner and the means of treatment, having been clearly described in recent years, are not within the province of the present essay.

This presentation is concerned with the relatively small group of childless couples who, having been thoroughly studied and, perhaps, treated, find themselves in the unhappy estate of unilateral barrenness—a dilemma in which the female is theoretically fertile and the male alone is absolutely sterile. Is it the privilege of such unblest women, lucklessly mated to sterile husbands, to achieve maternity artificially? The moral and legal aspects of this question are, for the present, difficult to crystallize, but from the physiologic viewpoint the response is unequivocally affirmative. It

must, nevertheless, be admitted that it is well-nigh impossible to apply the medical answer without due consideration to the two imponderable components of the question.

If an absolutely irremediable barrier to fertilization is found in the husband and if the wife, after complete study is potentially fertile it is then incumbent upon the physician to explain the hapless predicament to the barren couple. The physician should not attempt to sway the judgment of the couple but should merely discuss with them the need of adjusting their material philosophy to that of a childless union, or, if they so please, the advisability of adopting one or more children. Occasionally, it will be suggested by one of the partners that the wife submit to artificial impregnation or, as the lay magazines state, "have a test-tube baby." The physician need assume no particular responsibility if one of the first two courses is chosen, but his burden is, indeed, heavy should the couple elect the last mentioned procedure.

The occurrence of normal pregnancy following the artificial transfer of semen to the reproductive tract of the female is not a newly discovered phenomenon. The fourteenth century legend of the warring Arabian tribesmen who, in the dead of night, successfully inseminated the well-bred mares of their enemies with semen obtained from inferior stallions is often related as the origin of the procedure. The first successful experimental fecundations were those of Jacobi who, in 1700, was able to fertilize artificially the eggs of fish. Nearly a century later, the Abbe Spallanzani succeeded in artificially impregnating a spaniel bitch. The first successful artificial impregnation in a human female is credited by Home to John Hunter who allegedly related the occurrence of such a pregnancy following the transfer to the vagina of semen from a husband with hypospadias. In the United States, Marion Sims was the first to employ this modality in sterility. In 1866, Sims reported that 1 of 6 intrauterine inseminations had been successful. Since that time, as reviewed recently by Cary, many gynecologists have recorded their experiences with artificial impregnation. The procedure is currently in the limelight because of the keener interests in barren marriages and because, as knowledge concerning the menstrual cycle and ovulation accumulates, such inseminations are more often successful. The recent questionnaire survey of 30,000 physicians, conducted by the National Research Foundation for Eugenic Alleviation of Sterility, shows that at least 9000 live children were produced by artificial impregnation in this country up to June, 1940.

*Indications for Artificial Impregnation:* The Indications for artificial impregnation in instances of sterility though limited and well defined, vary with the type of insemination to be employed. The procedure may be either *homologous*, when the husband's semen

is artificially transferred to his wife's reproductive tract, or *heterologous*, when the semen of a stranger is employed.

Homologous insemination is indicated in the presence of either penile or vaginal malformations which prevent the normal deposition of semen in a couple otherwise potentially fertile. Thus, either hypospadias or pronounced vaginal atresia may constitute an indication for homologous insemination. A persistently acid reaction of the cervical mucus, as described by Guttmacher and Shettles, may be considered an indication for homologous insemination of the intrauterine type. The procedure is, however, of no value in the management of ordinary sterility wherein one attempts as Guttmacher states, "to give the spermatozoa a 3-inch boost on their 6-inch journey."

Heterologous insemination, utilizing the semen of a donor, is indicated when it has been positively determined that the husband is absolutely sterile, as in either total aspermia or irreparable azoospermia, and that the wife is potentially fertile. The later statement implies definite knowledge that the Fallopian tubes of the wife are normally potent, that there is no cervical infection, and that the uterus is not underdeveloped. It is obviously important that the wife be free from any constitutional or local disorder which would make pregnancy hazardous. Heterologous insemination is the type usually employed, because absolute sterility of the male is more common than genital malformations of either partner. For this reason, certain prerequisites to its success, as well as the technique, are herein discussed.

*Moral and Legal Aspects of Heterologous Insemination:* The conditions imposed upon the physician who consents to perform artificial impregnation in a potentially fertile woman, with semen from a donor other than the husband, include the proper selection of couples in which such a procedure may be risked and the careful choice of a suitable donor.

In selecting the couples, it must be ascertained that both husband and wife are equally earnest in the request that artificial impregnation be performed and that both of them fully grasp the psychologic and emotional dangers which surround such a procedure. It is best to delay the proposed insemination for several months in order that the physician may assure himself that the husband's interest is not abnormally heightened by sheer bravado in an attempt to escape the self-accusations of inferiority. By thus familiarizing himself with the character of the husband, the physician is aided in his determination to avoid any future marital discord.

As a medicolegal safeguard, written permission for the impregnation should be obtained from both partners. The author does not deem it wise or necessary to establish all of the ceremonious legal

formalities which Seymour and Koerner suggest. Several possible legal charges have been mentioned by both lay and medical writers as constituting serious obstacles, namely, a violation of the law by all concerned, the crime of adultery by the wife, and the aspersions of bastardy on the heir. There being no law, written or unwritten, concerning the legality of the act, the participation by anyone in the execution of artificial impregnation is not a statutory offence. The question of adultery is a debatable one, even though someone has said that "it is difficult to conceive of adultery being consummated in a test-tube." The common law, upon which most decisions concerning adultery would rest, considers adultery to be linked to the concept of sexual intercourse, an element lacking in artificial impregnation. However, as Beardsley points out, the Supreme Court of Ontario, in 1921, sustained a charge of adultery by stating, "The essence of the offence of adultery consists not in the moral turpitude of the act of sexual intercourse, but in the voluntary surrender to another person of the reproductive powers or faculties of the guilty person." If such a decision were generally upheld, it could be made to affect all women who submit to artificial impregnation.

The legitimacy of the child born of artificial impregnation is a delicate question. As a general rule, most statutes protect any child born in wedlock from the aspersions of bastardy. However, even though the presumption of legitimacy is one of the strongest presumptions of the law, it is not absolute under all circumstances. It is easily controverted by proof of the husband's sterility. Therefore, in order to avoid any future shadow of bastardy and to guard the property rights of the child, whose inheritance privileges may be challenged by greedy relatives, who by chance acquire knowledge of the manner of conception, it is best to establish protective measures at the time. The suggestion of Seymour and Koerner that, after pregnancy results from artificial impregnation, another physician one ignorant of the origin of the conceptus—be engaged to complete the obstetric care does not solve the problem. The advice of the Legal Bureau of the American Medical Association that the husband institute formal adoption proceedings as soon as the child is born, while certainly a safe course, seems to be unnecessarily public. Once a man has accepted a child born to his wife as his own, the law almost guarantees the legitimacy and, therefore, the inheritance of that child. Thus, in the author's opinion, the signed, witnessed consent of both marital partners for the performance of artificial impregnation, to which the husband has appended the affirmation that the child is his and his legal heir, constitutes sufficient legal protection for all concerned.

The selection of a donor entails the impersonal purchase by the physician of semen from a healthy, fertile male of good character

and favourable heredity—one who has no evidence clinical and serological, of ever having had either gonorrhœa or syphilis. The donor must, moreover, be unknown to the barren couple. The request by the couple that a member of the family be employed as the donor should be categorically denied. It is obviously important for esthetic, moral, and psychologic reasons to preserve the anonymity of the donor. It is best that the donor selected be of the same racial strain as the husband and, if at all feasible, possess some of his physical characteristics.

*Technique of Artificial Impregnation.*—The success of any insemination hinges on the potential fertility of the wife, as previously mentioned, on the excellence of the donor's semen, and on the timing of the insemination. The manner of introducing the semen into the vagina is the simplest part of the procedure. The donor is instructed to obtain the semen by manual masturbation, collecting it in sterile, dry, glass vial and keeping it at room temperature until used. The semen should be introduced into the recipient as soon as possible after its collection, certainly within an hour. The specimen should be examined microscopically, as a check, when it is received from the donor.

The wife is advised to have intercourse with her husband if he has no pyospermia, just prior to reporting for the insemination, with the hope that an imminent ovulation may be hastened and that favourable cervical secretions will be stimulated. If intercourse with her husband is not feasible, the woman is advised to take a preliminary vaginal douche with 25 per cent. solution of sodium bicarbonate. The temporary alkalinity of the vagina thus achieved may enhance the fertilizing ability of the spermatozoa. With the patient in the usual lithotomy position and the table tilted to the Trendelenburg angle, the specimen of semen is then merely squirted against the external os without exposing the cervix. For this purpose, it is convenient to use a sterile, dry, glass syringe and a blunt, 16-gauge needle. The patient is kept on the table in the Trendelenburg position for 30 minutes and is then permitted to follow her customary duties.

There is nothing to be gained, in the author's experience, by introducing the semen directly into the uterine cavity through a small rubber catheter or a Keyes-Ultzmann cannula. In fact, the results of the intrauterine method may be inferior because of the expulsive contractions of the uterus evoked by stimulation of the internal os. It is imperative, when the intra-uterine technique is employed, to allow the uterine spasm caused by the passage of the catheter or cannula to subside before introducing no more than 0.5 cc. of the semen. A larger quantity of the semen tends to distend the uterine cavity and may give rise to undesirable contractions.

The timing of the artificial insemination so that it coincides with ovulation is obviously of paramount importance. When the wife is able, because of either habitual midcycle pain or cyclic expulsion of clear cervical mucus, to foretell accurately the time of ovulation, the problem is simplified. If, however, no signs suggestive of ovulation are available, as is usually the case, 2 or 3 inseminations during the mid-portion of a single cycle should be performed. When failure occurs, even after such multiple inseminations, the days of the cycle selected should be altered at the next trial. In one of the successful cases reported, for instance, pregnancy did not occur after inseminations on the 11th and 14th days of the menstrual cycle but did follow subsequent inseminations on the 12th and 15th days. It is obvious that a large element of chance is involved in the meeting between a highly fertile ovum and a spermatozoon of similar quality. Seymour and Koerner recently reported that the average number of inseminations successfully employed by more than 4,000 physicians was 12. This number of attempts was distributed in many ways, such as 1 inseminations per month for 12 months, 2 inseminations per month for 6 months, and so forth. It is significant that 124 physicians reported successful artificial impregnation after as many as 21 inseminations. The patient, donor, and physician must be prepared, therefore, to repeat the procedure many times before meeting with success. The patient and donor will be more co-operative, if this is explained prior to the undertaking.

The recent observations of Guttmacher and Shettles on the cyclic penetrability of the cervical mucus to spermatozoa may obviate the necessity of multiple inseminations. These authors recommend the application of a micro-technique for the repeated study of the penetrability of cervical mucus and record several successful inseminations during the so-called optimal phase of maximum spermatozoal penetration. The method described appears to deserve future study and trial.

(*American Journal of the Med. Science, July, 1941*).

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### Extracts.

#### SODIUM SULFATHIAZOLE IN THE TREATMENT OF INFECTIONS OF THE URINARY TRACT

E. N. Cook, M. D., M. S. in Urology, Section on Urology: During the past five years urologists have been presented with many derivatives of the sulfonamide compounds for clinical trial. Numerous forms of sulfanilamide, then sulfapyridine, and, more recently, sulfathiazole have been used. I wish to report briefly concerning recent studies with sodium sulfathiazole. This work was carried out with the co-operation of Dr. Pool.

The advantages of this form of the drug over its parent substance are: (1) it is more rapidly absorbed, and (2) it is less toxic. As it is absorbed more rapidly it also is excreted more rapidly. It was felt that perhaps this fact would hinder generally the building up of an adequate concentration of the drug in the blood and urine. This was not found to be the case. Early in the work on the sulfonamide compounds at the Clinic we advocated the use of much smaller doses than were used elsewhere in treating infections of the urinary tract. During the past year the experimental work of Dr. Helmholtz has corroborated the early clinical observations. In spite of more rapid excretion of sodium sulfathiazole, we have been able to maintain in the urine an adequate bacteriostatic and bactericidal concentration at all times. In cases of impaired renal function this drug can be used more easily than can other sulfonamide derivatives.

The drug was given to approximately 200 patients who had infections of the urinary tract. These patients were not selected. Every type of organism was present as well as all types of pathologic change. The gramnegative bacilli respond equally well except the *Pseudomonas*, which is most obstinate to treatment. The gram-positive cocci, with one exception, all respond satisfactorily, particularly the staphylococci and micrococci. The *Streptococcus faecalis* did not respond to this drug, which indicated again that this organism is resistant to the sulfonamide compounds. Certain coexisting pathologic changes, such as tumor, calculi and obstruction, will definitely inhibit the action of the drug. This has been found to be true of all other urinary antiseptics.

We have used a dose of 20 to 60 grains (1.3 to 4 gm.) daily, and more recently it has not been more than 30 grains (2 gm.). The drug is given for a period of six to ten days.

Toxic reactions have been almost nil—a few patients have complained of nausea, which usually disappeared in twenty-four to forty-eight hours. Skin reactions were absent except in two cases.

In both of these cases the drug apparently produced reactions manifested by fever, general malaise, headache and nausea, as well as by dermatitis. The administration of the drug had to be discontinued in these cases. In very few patients was there any elevation of temperature. In the first twenty cases in which the drug was given, blood studies were made but showed no change.

The interesting observation after a clinical trial of sodium sulfathiazole was the rather rapid relief of symptoms that occurred after its administration. Given to a patient suffering with burning, frequent micturition and dysuria, the drug will bring about a complete or almost complete relief of symptoms in twenty four to forty-eight hours in most instance. Personally, I believe that the rapid absorption and excretion are responsible for this rapid relief of symptoms.

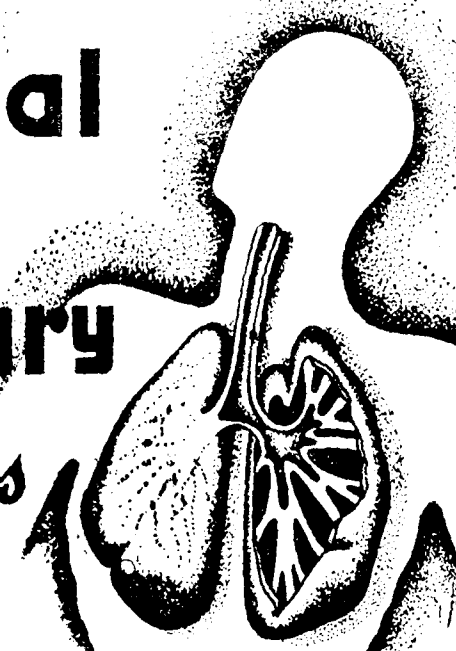
#### TREATMENT OF CONVULSIONS IN CHILDHOOD.

Peterman gives outlines of treatment of convulsions in childhood: If convulsions are due to fever, the fever must be reduced with cool packs. Hot baths should not be used unless there is a subnormal temperature. Cool enemas may be used. Chloroform may be administered. Chloroform is better than opium, as the latter depresses the respiratory centre and inhibits peristalsis. In place of chloroform a 50 per cent. solution of magnesium sulphate may be given as an enema or by mouth. A 20 per cent. solution may be given intramuscularly, even intravenously if given slowly. Phenobarbital is too slow in action for immediate effect. Spinal puncture is always indicated to rule out meningitis and other disease. The convulsions of tetany require calcium; those of tetanus require avertin. Status convulsivus usually is fatal unless treated with chloroform or magnesium sulphate. In chronic convulsions as the result of brain injury, phenobarbital may be given over a long time. In idiopathic epilepsy phenobarbital may be used as a specific for therapeutic trial. If the patient does not respond, he probably has an organic lesion. Phenobarbital is only a symptomatic treatment. Epilepsy should be treated by diet (high fat), rest, and regulation. No drug has any effect upon petit mal in children. Nearly one-half of the cases of epilepsy start as petit mal. Fasting and ketogenic diet will control one-half of the petit mal cases.

Smith summarizes the routine orders for convulsions on the Children's Medical Service of Bellevue Hospital as follows: (1) Patient admitted during a convulsion: (a) chloroform 1 or 2 drops

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at a time on mask, with plenty of air; (b) if twitching persists sodium amytal intravenously very slow until patients relaxes. (Maximum dose, 0.04 gr. per pound). (2) As soon as convulsion ceases: (a) magnesium sulphate, 25 per cent. from 5 to 10 c.c. intramuscularly; (b) lumbar puncture for diagnosis and relief of pressure; (c) Soapsuds enema; (d) one-half hour after enema sodium bromide 0.75 gr. per pound, and chloral hydrate, 0.1 gr. per pound by rectum, to be retained; (e) if temperature is 104°F. or more, aspirin, 0.1 gr. per pound by mouth as soon as patient can swallow; (f) calomel 0.1 gr. every 15 minutes for six to eight doses. In morning, milk of magnesia 30 c.c.; (g) laxative each night thereafter; (h) Sodium bromide, 0.125 to 0.25 gr. per pound every six hours for forty-eight hours. (3) Patient admitted with definite history or recent convulsion is treated as in No. 2. It is physician's duty to prevent second convulsion, in which there may be cerebral hemorrhage or other accident. (4) Chronic epileptics, after an attack: (a) enema, laxative; (b) bromide by mouth, one or two doses, (c) phenobarbital, 0.25 to 1 grain t. i. d.

(The Journal of Pediatrics, July 1940).

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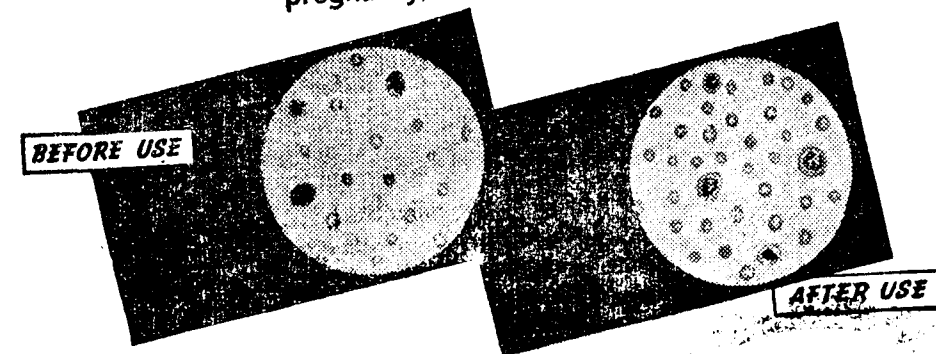
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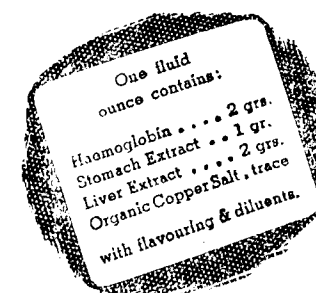
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MARCH 1942

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**PROBLEMS ARISING IN THE CHEMOTHERAPY OF  
PNEUMONIA AND MENINGITIS.**

HARRY F. DOWLING, M.D.,

*Clinical Professor of Medicine, George Washington University School of  
Medicine.*

Every new method of treatment brings its problems as well as its advantages. "Blitzkrieg" drugs may advance the patient rapidly and far toward recovery, but they expose him to new dangers, and by the very speed and comprehensiveness of their action change the picture of the battle so completely that the physician-strategist is at a loss to tell who is winning and on what front. Such is the story of the treatment of pneumonia and meningitis with the sulfonamides. Accordingly, I should like to discuss some of the problems which commonly arise, in the light of the experience of my colleagues and myself in the Pneumonia Control Program of the District of Columbia and on the wards of the Gallinger Municipal Hospital. The use of these drugs will be considered in the following order:

1. When should the sulfonamides be used?
2. Which drug should be selected for a particular type of case?
3. How should the drugs be used?
4. When should they be stopped?
5. What additional measures should be used in conjunction with the sulfonamides?

The first problem that presents itself is, "When should the sulfonamides be used?" It is common knowledge that these drugs are of value in infections caused by pneumococci, beta hemolytic streptococci, staphylococci and meningococci. They are probably helpful in Friedlaender's bacillus and Hemophilus influenzae infections. The common cold influenza, and the atypical pneumonias presumably due to a virus or Rickettsiae do not seem to be influenced by any of the sulfonamide drugs. This is apparently true also of benign lymphocytic choriomeningitis, encephalitis, poliomyelitis, and a host of other virus diseases of the nervous system.

The indications for giving the sulfonamides thus become evident. Since pneumococci and hemolytic streptococci cause by far the greatest number of pneumonias, the sulfonamides may be administered whenever there is reasonable evidence that pneumonia is present. A specimen of sputum for typing and some blood for culture should always be collected before the first dose of the drug is given. Then, if specific causative organisms are not found, and if the clinical and roentgenographic appearance of the disease resembles that of the so-called virus or Rickettsial pneumonitis, the sulfonamides may be stopped before they have had much opportunity to cause drug fever or any other complication which might confuse the clinical picture or harm the patient.

The contraindications to the sulfonamides are not as clearly defined. There is no doubt that they should be withheld entirely in the presence of marked liver disease. When anemia, leukopenia, or renal disease are present, it is our practice to administer the drugs cautiously, checking the blood or urine at least once a day and following the clinical condition of the patient very closely.

The sulfonamides are indicated in meningitis when the causative agent is the meningococcus, the pneumococcus, the hemolytic streptococcus, or the influenza bacillus. When meningitis is suspected, a lumbar puncture should be performed immediately, followed by a leukocyte count and a Gram stain of the cerebrospinal fluid. Pneumococci, meningococci, and influenza bacilli can be typed directly from this fluid by the Neufeld technic. If organisms are found, the appropriate sulfonamide may be given at once.

This brings us to the second problem: "Which drug should be given?" When the records of the 644 cases of pneumococcal pneumonia treated at Gallinger Municipal Hospital in the past 2½ years are examined (table 1), it is seen that the mortality rates are very

TABLE I.  
*Results of Treatment of Pneumococcal Pneumonia with Sulfonamides (1938-1941.)*

| Pneumococcus Type                 | Sulfapyridine |               | Sulfathiazole |               | Sulfadiazine |               | All cases    |               |
|-----------------------------------|---------------|---------------|---------------|---------------|--------------|---------------|--------------|---------------|
|                                   | No. of cases  | Died          | No. of cases  | Died          | No. of cases | Died          | No. of cases | Died          |
| I                                 | 84            | 7             | 12            | 2             | 40           | 2             | 136          | 11            |
| II                                | 32            | 1             | 4             | 0             | 4            | 0             | 40           | 1             |
| III                               | 69            | 17            | 3             | 1             | 11           | 4             | 83           | 22            |
| V                                 | 9             | 0             | 4             | 0             | 6            | 0             | 19           | 0             |
| VII                               | 45            | 4             | 8             | 0             | 17           | 2             | 70           | 6             |
| VIII                              | 34            | 4             | 7             | 1             | 6            | 0             | 47           | 5             |
| Other Types                       | 153           | 27            | 47            | 6             | 49           | 6             | 249          | 39            |
| Bacteremic Cases (included above) | 77            | 21<br>(27.3%) | 12            | 4<br>(33.3%)  | 17           | 5<br>(29.4%)  | 106          | 30<br>(27.6%) |
| Total Cases.....                  | 426           | 60<br>(14.1%) | 85            | 10<br>(11.9%) | 133          | 14<br>(10.5%) | 644          | 84<br>(13.0%) |

nearly the same for each of the sulfonamide drugs used (14.1 per cent., 11.9 per cent. and 10.5 per cent. for sulfapyridine, sulfathiazole and sulfadiazine, respectively). On the other hand, table 2

TABLE 2  
*Frequent Toxic Reactions Observed Following the Use of Certain Sulfonamides.*

| Toxic Reaction         | Sulfapyridine<br>(372 Patients) | Sulfathiazole<br>(100 Patients) | Sulfadiazine<br>(165 Patients) |
|------------------------|---------------------------------|---------------------------------|--------------------------------|
|                        | per cent.                       | per cent.                       | per cent.                      |
| Nausea and Vomiting... | 21.8                            | 12.0                            | 3.7                            |
| Anemia or Leukopenia.  | 4.6                             | 2.0                             | 3.0                            |
| Toxic Psychosis ...    | 2.7                             | 3.0                             | 2.4                            |
| Dermatitis ...         | 2.2                             | 12.0                            | 0.6                            |
| Renal Lithiasis ...    | 1.9                             | 2.0                             | 0.0                            |

demonstrates that there are marked differences in the percentages of toxic reactions occurring with each of these drugs. Vomiting occurred in 21.8 per cent. of the patients receiving sulfapyridine, in 12.0 per cent. of those receiving sulfathiazole, and in 3.7 per cent. of the ones receiving sulfadiazine. There was practically no difference in the percentage of hematologic complications caused by each of these 3 drugs, and the incidence of delirium was about the same among the patients receiving any of them. Sulfapyridine and sulfathiazole were responsible for the formation of kidney stones in 1.9 per cent. and 2.0 per cent. respectively, while no instance of kidney stone was noted among the 165 patients treated with sulfadiazine. The presence of kidney stone was determined by the observation of gross hematuria (or a marked increase in the number of red blood cells seen microscopically), accompanied by pain in the flank and usually by a rise in the blood urea nitrogen. Sulfonamide calculi are usually not visible by means of X-ray films. Dermatitis followed the use of sulfapyridine in 2.2 per cent. of the patients and of sulfathiazole in 12.0 per cent. It was observed in only 1 patient who received sulfadiazine.

From the foregoing data, it is evident that the choice of the drug to be used in pneumonia depends not so much upon therapeutic efficiency, since sulfapyridine, sulfathiazole and sulfadiazine are similar in this respect, but upon the toxic reactions anticipated. In view of its low toxicity, I believe that sulfadiazine is the drug of choice in the treatment of pneumococcal pneumonia. Sulfathiazole is to be preferred over sulfapyridine since nausea and vomiting are less frequent when the former drug is used. It must be emphasized, however, that any one of them can be used (1) if another is not

available, or (2) if the patient has shown toxic effects from the previous administration of one of the others.

Sulfanilamide and sulfapyridine are both effective in pneumonia caused by the *Streptococcus haemolyticus*, and although sulfathiazole and sulfadiazine have been tried in only a few cases, they apparently work well also. When a patient is suffering from pneumonia caused by the influenza bacillus or the Friedlaender bacillus, any of the sulfonamides may be tried, although their effectiveness is doubtful.

In meningitis, the choice of drug depends upon its penetration into the cerebrospinal fluid. Sulfapyridine and sulfanilamide are superior to sulfathiazole in this respect. Preliminary studies have shown that sulfadiazine is well absorbed into the cerebrospinal fluid also, and Dingle, Thomas and Morton have reported 13 recoveries in 40 cases of meningococcal infection. It will be interesting to see whether further work will bear out these good results.

The third problem is, "How should the sulfonamides be used?" At present, most people having extensive experience in the use of these drugs believe that they should be administered so as to build up a high concentration in the blood or spinal fluid quickly. In patients with pneumonia, I prefer to obtain levels of 6 mg. per 100 c. c., if possible, in the case of sulfapyridine and sulfadiazine, and at least 4 mg. per 100 c. c. when sulfathiazole is administered. These high levels should be maintained until the temperature has been within normal limits for 3 or 4 days and the patient is clinically well. Then the drug should be stopped completely.

A satisfactory initial dose is 4 grams of sulfapyridine and 6 grams of sulfathiazole or sulfadiazine, followed by 1 gram of any of the drugs at 4-hour intervals, for an adult, and proportional doses for a child, on the basis of body weight. If any of these drugs cannot be given by mouth for any reason, the sodium salt may be administered intravenously in doses of 0.06 Gm. per kilogram of body weight. Subsequent doses cannot be given according to any arbitrary scale, but must be calculated after estimations have been made of the amount of drug in the blood. The sodium salt may be given as a 5 per cent. solution in distilled water, but I prefer to use it in 500 or 1,000 c. c. of physiologic saline solution, since in this way the blood level of the drug can be kept high during the time the entire amount of fluid is being slowly administered.

In patients with meningitis, the level of the drug in the cerebrospinal fluid should be kept at 4 mg. per cent or higher. This can usually be accomplished satisfactorily by oral or intravenous administration. After all evidence of the infection has disappeared and the spinal fluid is normal, it is still advisable to continue the administration of the drug for a period of 1 month to make certain that no recurrence occurs. Since several investigators have seen

severe cases of myelitis develop from the intrathecal administration of concentrated solutions of the sulfonamide drugs, the sodium salts of sulfapyridine and sulfadiazine, if administered at all, should not be given in any stronger than a 2 per cent solution.

It has been said that a good general knows when to retreat. Likewise, when the competent physician employs powerful drugs, he should be able to perceive instantly when he has gone too far, thus exposing his patient to a toxic reaction, and know when to stop the treatment and apply restorative measures. This represents the fourth problem in the use of the sulfonamide drugs—"when to stop them." The following indications apply both to cases of pneumonia and of meningitis. In the presence of acute hemolytic anemia, or a developing leukopenia, or acute hepatitis—conditions which are often fatal—it is imperative that all sulfonamides be stopped immediately and the complication be treated (table 3). When peripheral neuritis occurs, the use of the sulfonamide employed should be stopped, but it is permissible to change to another sulfonamide. When renal calculi, formed from acetylated sulfapyridine or sulfathiazole, occur, the use of the drug should be stopped immediately and fluids forced. If further treatment is needed, another sulfonamide may be administered, preferably sulfadiazine, if it is available, since no instance of this complication was found by us among 165 cases treated with that

TABLE 3.

*Toxic Reactions Indicating Cessation of Sulfonamide Therapy.*

| Toxic Reaction                     | Symptoms and Signs                                            | Laboratory Tests              | Significance                                                        |
|------------------------------------|---------------------------------------------------------------|-------------------------------|---------------------------------------------------------------------|
| Acute Hemolytic Anemia ...         | Pallor and weakness                                           | R.B.C. count                  | Stop drug immediately. Give no further sulfonamide therapy.         |
| Neutropenia or Agranulocytosis ... | Weakness                                                      | W.B.C. count and differential |                                                                     |
| Acute Hepatitis ...                | Rapidly developing marked jaundice, increase in size of liver | van den Bergh; Icterus index  |                                                                     |
| Peripheral Neuritis ...            | Pains, paresthesias absent or diminished reflexes             | None                          | Change to another sulfonamide if further therapy is needed          |
| Dermatitis ...                     | Erythematous, nodular, or urticarial rash                     | None                          |                                                                     |
| Drug Fever ...                     | Continuous or remittent fever                                 | None                          |                                                                     |
| Renal Calculus ...                 | Hematuria, flank pain, usually retention of urea              | Urinalysis                    | Continue same drug, parenterally if necessary, or change to another |
| Nausea and Vomiting ...            | Nausea alone, or with vomiting                                | None                          |                                                                     |

compound. Since dermatitis and drug fever usually not necessary to employ another sulfonamide, but it is probably safe to do so if the need requires it. Nausea and vomiting are not serious symptoms. The drug which caused them may be continued or a change may be made if the symptoms cannot be controlled. The indications for discontinuing the drugs when the patient has recovered from pneumonia or meningitis have already been discussed.

The fifth problem introduces the question: "What measures should be used in conjunction with sulfonamide therapy?" In the first place it must be emphasized that the patient is being treated, not merely a mass of bacteria lodged in an inaccessible organ. Supportive and symptomatic treatment, including oxygen therapy, relief of distention, and digitalization for congestive heart failure, should not be neglected. The proper use of serum in addition to the sulfonamides has been much discussed as it pertains to pneumococcal pneumonia. On the basis of mortality rates observed in a series of alternated cases, 12.6 per cent in 80 patients treated with sulfapyridine and 9.8 per cent in 82 patients treated with serum plus sulfapyridine, I believe that serum should be given to patients over 40 years of age, or to patients in need of an immediate defervescence, as soon as typing of the sputum reveals the pneumococcus to be the causative organism, unless the disease appears to be very mild as judged by all the combined clinical and laboratory evidence. Bullowa and his associates and Plummer and his co-workers obtained no better results when serum was given in addition to a sulfonamide than when the sulfonamide was given alone. In these two series, however, treatment with the drug was started before sputum typing was completed, serum being given later to every alternate case. In our series, all treatment was withheld until a type of pneumococcus was obtained, and then either the drug or the drug plus serum was given to each alternate case. It is reasonable to conclude that this difference in method may account for the poorer results obtained by the other groups with the use of combined serum and sulfonamide therapy. In addition to the comparatively small group of patients who should be started off with the combined treatment, there are other patients who do not respond well to the drug. If a patient has not responded favorably to sulfonamide treatment within 24 to 48 hours, in spite of adequate levels of the drug, the clinician should consider administering serum immediately, since the value of serum is in great part dependent upon its being given within the first 4 or 5 days of the disease. Serum is needed today in only a fraction of the cases in which it would have been used before the advent of sulfonamide therapy, but when it is needed, it should be given promptly, and in sufficient doses. Administered in this way, it is often a life-saving measure.

In pneumococcal meningitis, serum is always given intravenously along with sulfapyridine or sulfadiazine. The initial dose of serum should be at least 200,000 units, and doses of 50,000 to 200,000 units should be administered daily thereafter as long as they are needed. Some observers believe that it is not necessary to give serum intrathecally. If it is so given, 50,000 units are usually administered along with 5 c.c. of fresh human serum in order to supply complement.

Whether to use serum in addition to the sulfonamides in meningococcal meningitis is a disputed question. Although the results of experiments in animals seem to show that combined treatment is superior to treatment with the sulfonamides alone, conclusive results have not been obtained in humans. Until the matter is settled, I prefer to combine the sulfonamides with serum.

The results in meningitis caused by *Streptococcus haemolyticus* are excellent with the use of sulfanilamide or sulfapyridine alone, while in influenzal meningitis the use of serum in addition to the sulfonamides is probably the best policy.

In conclusion, it might be said that the weapons have been forged and placed in our hands. It is up to us to know how to use them. We should know when to employ the sulfonamide weapons, which weapon should be selected, how it should be used, what other weapons should be employed at the same time, and when the use of the weapon should be discontinued. The proper knowledge of these new weapons should mean a campaign against death, the like of which the world has never seen.

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## CLINICAL ASPECTS OF VITAMIN DEFICIENCY IN THE EAR, NOSE AND THROAT.

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The manifestations of true deficiency diseases are so rare in the ear, nose and throat that on first thought vitamins may not be considered important. Specialists are often criticized for a too narrow outlook. It is well to review the field of avitaminosis, to see if there are diseases ordinarily ascribed to other causes that may be due, at least in part, to insufficient vitamin intake.

### VITAMIN.

This has been called the anti-infective vitamin, a term given by Mellanby in 1926 because of the chronically infected noses and

frequent upper respiratory infections he found in infants on A deficient diets. Widespread advertising has furthered this anti-infective idea among the public. Vitamin A preparations are given routinely to the personnel of large companies for the prevention of colds.

The experimental evidence is found in animals fed deficient diets and from clinical studies of its use on large control groups.

In an important study in 1925 Wolbach and Howe fed rats Vitamin A deficient diets. The epithelium of the upper respiratory tract and sinuses underwent a metaplasia from the normal ciliated columnar to a keratinized, stratified squamous type, followed by infection. This has been verified by many other workers and all find animals on A deficient diets develop infections of the upper respiratory tract.

There have been numerous clinical studies of the effect of vitamin A and colds.

Some merely give a vitamin concentrate, and the number of colds was recorded, compared with the number the subject thought he had the year before. Others compare the results with the similar group as controls.

One of the best of these studies was by Jeghers on 162 medical students, 50 or 36 per cent. were found to have sub-normal light adaption and their calculated vitamin intake was  $\frac{1}{2}$  of the other. The incidence of colds was about the same, though the duration was longer in the vitamin deficient group. Others gave an excess of vitamin A to groups already known to be receiving an adequate intake. There was no lowered incidence of colds but a suggested shortening of duration and lessened severity.

No systemic lack of immunity or anti-body production has been demonstrated in Vitamin A deficiencies.

The present status of vitamin A in the ear, nose throat may be summarized:

1. Vitamin A is necessary to the health of the mucus membrane of the upper respiratory tract. When deficient, there may be lowered local resistance to bacterial infection.

2. The epithelial metaplasia in experimental animals is a late result, it is *not* seen in humans with rare exceptions. The stratified squamous epillum in atrophic rhinitis has been compared to the metaplasia of animals. This disease has long been thought to have a dietary etiology. Its rarity, even in clinics today, suggests better feeding, especially of infants.

3. There is no special characteristic of infections in the ear, nose and throat that identify it as due to lack of vitamin A. Neither do we have a simple method of determining the presence of A deficiency. A calculation from the diet may help. Blood level

determinations or dark adaptation tests are not practical for routine office of clinic use.

4. Insufficient intake of vitamin A may be one factor to be considered, along with allergy, infection, humidity and many others in persons subject to frequent colds.

5. The administration of vitamin A to persons already receiving an adequate intake in the diet does not lessen susceptibility to colds. It may shorten their duration or lessen their severity.

6. The term anti-infective vitamin is not justified.

#### VITAMIN B.

Including B<sub>1</sub> thiamin chloride, and other factors of the B complex.

One of the known changes in B deficiencies is the nerve degeneration, specifically de-mylenization. Possible applications that suggest themselves in otolaryngology are in diseases of the 8th nerve, in the cochlear division, deafness; and the vestibular portion, vertigo; as well as the many forms of neuralgia about the head.

*Eighth Nerve.* It has been shown that experimental animals (chicks, rats) on diets lacking in various factors of the B complex, undergo degeneration, demylenization of both the cochlear and vestibular nerve.

Selfridge has written extensively on both the experimental and clinical aspects of vitamin B complex deficiency as a factor in the cause of nerve deafness. He grants it is often a senile change, but feels that the degeneration of age is caused or accentuated by vitamin deficiency. He offers a large series of cases, with audiograms before and after treatment, showing definite, though not marked, improvement in hearing in many after administration of various factors of the B complex. There is nothing distinctive in the audiograms to indicate the cases as different from the usual primary nerve deafness. Other observers have reported similar studies with poorer results.

I have been interested in a series of nerve deafness cases treated by a colleague with vitamin B, in large doses with entirely negative results. There was no improvement of hearing in the case of nerve deafness which I have treated with B.

It is difficult to believe that mild, sub-clinical avitaminosis is a real factor in nerve deafness, when we remember defective hearing is not a symptom of the definite B deficiency diseases, beri-beri or pellagra. Tinnitus and vertigo have been described in pellagra however.

The changes observed in animals in the vestibular nerve have suggested the use of B<sub>1</sub> and B complex in Menieres syndrome. Harris and Moore noted peculiar dietary habits in persons with Menieres disease. Large doses of thiamin were ineffective. Then they tried nicotinic acid with negative results. Used together, 250 milligrams of nicotinic acid and 20 milligrams of thiamin per day, 17 of 20 cases

were entirely relieved, 3 improved. In 10 the tinnitus disappeared and was improved in the others. In 12 the hearing was improved.

Atkinson divides Menieres case into those due to allergy and those due to vascular spasm. The latter are mostly in older individuals and respond to B and nicotinic acid. He feels the improvement is due to a vaso-dilator action, rather than the correction of vitamin deficiency.

Cases of pain about the head, over the sinuses, nose, face and throat without apparent disease are frequent in oto-laryngology. These have been most difficult to handle, they are often labeled as "neurotics." The use of Thiamine Chloride has been a distinct advance and worth a trial before alcohol injections or surgery. Fifty milligrams of Thiamine Chloride subcutaneously daily for 10 days is an adequate trial. The relief may be due to correcting of a deficiency or some "non-specific" action of B as some feel.

The lesions in the mouth, tongue and pharynx in pellagra and those of the lips, cheilitis, in riboflavin deficiency should be mentioned.

To summarize B<sub>1</sub> and B complex in oto-laryngology:

1. There is no disease syndrome in the ear, nose, or throat characteristic of B deficiency.
2. Good results have been reported in its use in case of nerve deafness and Menieres disease. Its use empiracally in these cases may be justified.
3. Its use in the troublesome and baffling neuralgias about the sinuses, throat and head is justified. It is simple, easily given, relieves many of these that otherwise would need alcohol injections or more drastic surgery.

#### VITAMIN C.

Ascorbic or Cevitamic acid. The classic manifestations of a lack of vitamin C is scurvy. This disease will not be discussed here, though it may be necessary to recognize or differentiate its oral manifestations in laryngology.

Hemorrhage from the nose may also be a symptom even in so called sub-clinical scurvy.

With the exception of scurvy, there are no characteristic conditions of the ear, nose or throat typical of vitamin C deficiency.

#### VITAMIN D.

Vitamin D is known to control bone metabolism by the utilization of phosphorus and calcium. The disease in oto-laryngology where bone metabolism is important is otosclerosis. Lesions in the labyrinth similar to otosclerosis have been reported in experimental animals on a diet deficient in vitamin A and D.

Clinically there is no evidence that a lack of vitamin D is a causative factor in otosclerosis or that its administration influences its progress.

#### VITAMIN K.

The beneficial effect of vitamin K in hemorrhage is in cases due to lack of prothrombin, usually associated with a lack of bile salts. Surgery of the ear, nose or throat is not often necessary in jaundiced individuals. A lack of prothrombin has been shown after massive hemorrhage. Further studies may show the value of vitamin K in hemorrhage such as severe tonsillar or nasal.

#### SUMMARY AND CONCLUSIONS.

1. It is assumed that an adequate vitamin intake is necessary for general bodily welfare and therefore to the normal state of the ear, nose and throat.
2. We must be critical of adapting to humans the findings in experimental animals fed on diets deficient in the various vitamins.
3. Diseases of the ear, nose and throat characteristic of avitaminosis are rare. However, it may be a contributing factor in a number of conditions ordinarily considered due to another etiology.
4. The use of vitamin preparations is worth trial clinically in a number of ear, nose and throat conditions, even though no definite lack of intake is shown.

(Illinois Medical Journal, October 1941).

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## THE ACUTELY ILL CHILD A CLINICAL CONSIDERATION

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The scope of this subject is so broad that space necessarily limits the discussion to only the brief essentials.

### ETIOLOGY.

While the possible causes of acute febrile illness in childhood are almost innumerable, there are certain conditions that are seen frequently which embrace perhaps 95 per cent of cases. In order of approximate frequency these are:

1. Acute upper respiratory infection.
2. Communicable disease.
3. Urinary tract infection.
4. Enteritis.
5. Pneumonia.
6. Miscellaneous conditions.

Among the respiratory group, nasopharyngitis, pharyngitis, tonsillitis and otitis media are exceedingly common. Less often one encounters adenitis, sinusitis, bronchitis and mastoiditis. The list of communicable diseases is long and varies greatly throughout different sections of the country. Worthy of mention is the decreasing incidence of smallpox, typhoid and diphtheria. Acute pyelitis, pyelocystitis, and pyelonephritis are all frequent, while perinephritic abscess and hemorrhagic nephritis are relatively uncommon. Although not occurring with the alarming frequency of some years ago, enteritis continues to be quite prevalent, especially in infants. Most of these cases of diarrhea are of the so-called parenteral type and are secondary to acute infection elsewhere, usually of the respiratory tract. In the miscellaneous group the most important are the rheumatic syndrome, exanthem subitum, mesenteric adenitis, appendicitis, septicemia, pyemia and osteomyelitis.

Finally, there are certain associated conditions whose presence during acute infection may readily convert a pyrexia of moderate degree into a hyperpyrexia. Constipation, notably in infants and young children, falls into this category and this is also true of teething. Dehydration complicating infection often accounts for alarming temperature elevations as does active vaccination.

### DIAGNOSIS.

The child, acutely ill, may present problems which challenge our diagnostic acumen to the utmost.

#### A. General Considerations:

Age is an extremely important factor in diagnosis. Measles, diphtheria, scarlet fever and poliomyelitis are very rare under six months of age. Appendicitis seldom occurs in the very young. Hemorrhagic nephritis and acute rheumatic infections are relatively uncommon during the first two years of life whereas enteritis and exanthem subitum are very frequent at this age. While pyelitis may occur at any time it is, for the most part, a disease of the diaper stage.

In considering fever, per se, it should be remembered that children develop high fever more rapidly and more readily than adults, and that infants respond to infections with a hyperpyrexia more often than children. On the other hand, fever in infants and children is apt to subside with more rapidity than in adults.

Familiarity with the individual child is often of great assistance in evaluating the degree and severity of infection present—i.e., some children repeatedly react to trivial infection with temperature elevations of 103 or 104, whereas in others that amount of fever indicates a more severe illness. Further, some children tolerate high fever very badly and vice versa. This is well exemplified by the child who reacts with a convulsion each time the temperature reaches a certain elevation.

Given an *infant* with a high fever in which the physical examination is entirely negative, the most likely possibilities are exanthem subitum and pyelitis.

An intermittent fever is suggestive of otitis media or pyelitis—more rarely, sepsis, or one of the more unusual conditions such as undulant fever or malaria. In infants and young children, chills are rare and except for their occasional occurrence in exanthem subitum, pyelitis and malaria, usually signify the presence of sepsis.

#### B. Special Considerations:

1. Upper respiratory infections are usually quite apparent except in the neonatal period. Examination of the ears should never be neglected. Many physicians fail to appreciate the fact that in small children a moderate amount of throat inflammation may produce a high temperature. Respiratory infections frequently occur in combinations such as pharyngitis and otitis or tonsillitis and adenitis and when this exists hyperpyrexia results. Postnasal infections are more difficult to recognize. They are detected by including the child to gag and observing a mucoid or mucopurulent discharge in the hypopharynx. These children frequently have a nasal quality to the voice. All cases of throat infections presenting exudate demand a bacterial smear, a throat culture when possible, and specific inquiry as to diphtheria immunization and result of the Schick test. Contrary to the general belief, bronchitis (non-allergic) is uncommon in infancy and early childhood. While cough is a frequent symptom of upper respiratory infection in this group it

usually arises from throat irritation and postnasal drip rather than bronchial secretion and careful auscultation of the chest elicits rhonchi and not rales.

2. In pyelitis the age, sex and general appearance are all helpful. The child, usually female, is characteristically non-toxic and there is an absence of other signs and symptoms except possibly a reddened urethral orifice. Pyelitis often occurs in association with upper respiratory involvement and if one sees a child with a high fever and a mild respiratory infection, pyelitis should always be considered. In infants, local symptoms are uncommon and difficult to recognize. Older children practically always have an accompanying cystitis the symptoms of which predominate (frequency, urgency, dysuria, microscopic hematuria). They also may have abdominal or lumbar pain and chills.

The temperature curve of pyelitis is of the septic type although occasionally with a temporary urinary block, one finds a sustained fever until the obstruction is spontaneously relieved. In such cases the urine may be negative until the temperature drops.

Catheterized specimens for urinalysis are seldom necessary if the genitalia are carefully washed. In females, however, if cleansing is neglected vaginitis will frequently be diagnosed "pyelitis." The urine should not be centrifuged. It is to be stressed that a negative urine does not eliminate the possibility of pyelitis, as several urinalyses may be necessary before pus is found. A clean, uncentrifuged specimen showing more than an occasional leucocyte per high power field is good presumptive evidence of pyelitis.

3. Enteritis is characterized by frequent loose stools containing variable amounts of mucus, epithelial shreds, and undigested food particles. If to this picture is added the presence of pus and blood in the stool, dysentery should be suspected and stool cultures are indicated.

4. Pneumonia presents few difficulties in diagnosis except in its early stage. Most errors occur in misjudging the type of pneumonia present, which is determined for the most part by age. The pneumonia of infancy is of the lobular type whereas the pneumonia of childhood is usually lobar in distribution. Both of these are primary pneumonias due to the pneumococcus. Bronchopneumonia, in contrast, is secondary, and usually follows influenza, measles, and pertussis. Lobular pneumonia is often misdiagnosed "bronchopneumonia."

In infancy and childhood, the pathological process is reversed so that consolidation extends from periphery to hilus. It is thus apparent that bronchial breathing is a late sign and in early pneumonia the usual findings are suppression of breath sounds and perhaps an occasional shower of fine crackling rales at the end of inspiration. Deep breathing is necessary to elicit these changes so in small infants crying should be induced if necessary.

Pneumonia of the right lower lobe may be confused with appendicitis owing to the referred abdominal pain.

5. Meningitis. The incidence of all the meningitides is higher in childhood than in adult life and aside from the meningococcic (epidemic) type, influenzal, tuberculous and coccal meningitis are all fairly common. It should always be ruled out in any case of sustained fever and evident toxicity without adequate explanation. In small infants, signs of meningeal irritation such as neck rigidity, increased reflexes, pathological reflexes, etc., are frequently absent and there is toxicity, irritability, and lethargy progressing to stupor. If the fontanel is still patent, the presence or absence of bulging is of some diagnostic value, but in the final analysis, a diagnosis of meningitis in an infant or young child depends upon a healthy suspicion and a lumbar puncture. Convulsions occurring late in the course of any acute infection suggest the advent of a secondary meningitis or meningoencephalitis.

6. Exanthem subitum or roseola infantum is one of the commonest of the acute ailments of early childhood. It presents a striking picture that strangely enough has failed to receive the attention it warrants and as a consequence many of these cases go unrecognized.

The causative agent is unknown and, as observed in private practice, it is doubtful if the disease is contagious. Upon two occasions I have seen the condition limited to one of twins and have never observed secondary cases in a family. Age seems to be the important predisposing factor as the great majority of cases occur in infants of 10 to 18 months. It is rare after 2 years of age.

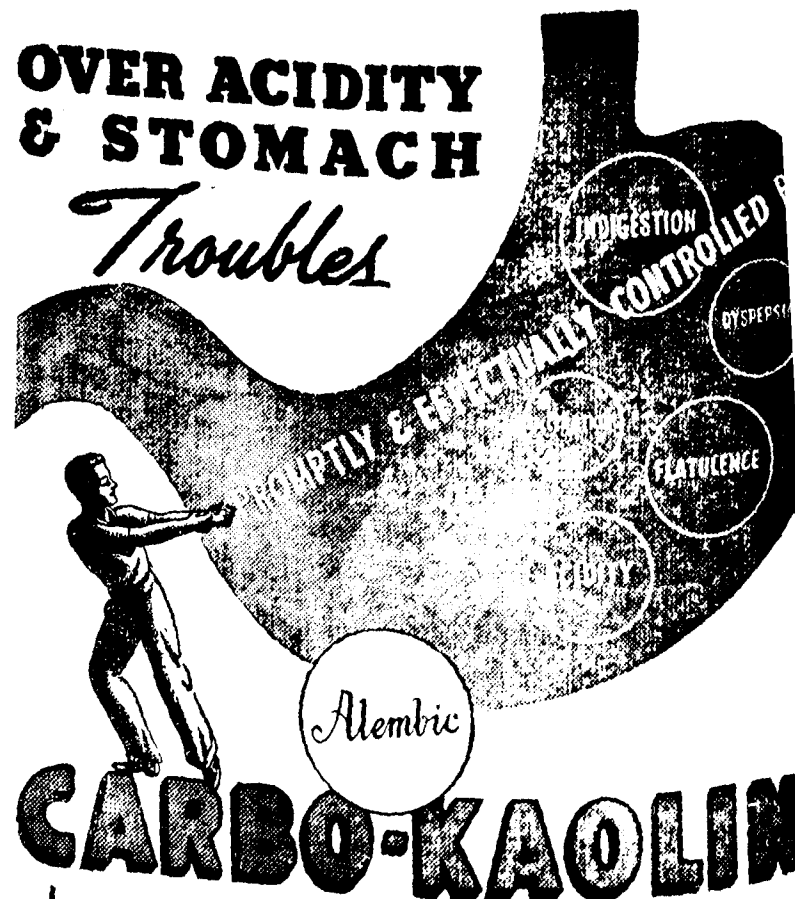
The onset is abrupt with a high fever ranging from 103 to 104 which continues usually without abatement for three or four days. During this period the infant is irritable and anorexic, but nothing is found on physical examination except evidences of slight upper respiratory involvement. The temperature then drops by crisis and within twenty-four to forty-eight hours a fine maculo-papular rash appears that last for about thirty-six hours. There is a leucopenia with a relative lymphocytosis.

Roseola infantum is most often confused with german measles or measles. In german measles the first symptom is usually the rash, while in measles the child has a prodromal catarrhal stage with fever that increases as the rash appears. In contrast, the infant with exanthem subitum is afebrile at the time of his eruption, there is no preceding catarrhal stage, and no Koplick spots or rash in the mouth are found.

7. Appendicitis in childhood runs a more variable course than in adult life and may present difficult problems in diagnosis. This is especially true of infancy as the symptoms are hard to evaluate and positive physical findings are difficult to elicit. The paramount

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## MEDICO-SURGICAL SUGGESTIONS

69

features include vomiting, abdominal pain, moderate fever, localized tenderness and leucocytosis. The temperature seldom exceeds 102.8 and very occasionally may be normal throughout. Examination of the abdomen should be the initial procedure for unless the child is quiet, localized tenderness and rigidity are detected with difficulty. Likewise, rectal examination usually adds very little unless there is co-operation. Leucocytosis and neutrophilia are usually present but are not invariable, and equivocal blood counts are quite common.

While serial observations are often helpful, an attitude of watchful waiting should not be overdone as temporization may lead to perforation. In infants and young children perforation sometimes occurs with amazing rapidity. Should the diagnosis be in grave doubt it is far better to remove a normal appendix than one which has ruptured.

8. The syndrome of abdominal pain in association with respiratory infection.

The commonest cause of abdominal pain in childhood is acute infection of the upper respiratory tract, particularly postnasal, pharyngeal or tonsillar infections. The term "mesenteric adenitis" has unfortunately been rather loosely applied to these cases but actually there is seldom and demonstrable mesenteric involvement. The mechanism of the pain remains obscure although a logical sequence of events would appear to be infection, impaired digestion, increased intestinal fermentation and gas pain.

The pain is usually colicky in nature and rather diffuse, although occasionally it may be localized over areas of gas. Nausea and vomiting are infrequent unless fluid or food has been urged injudiciously. The fever and leucocyte count vary, depending upon the severity of the accompanying respiratory infection. Palpation discloses superficial abdominal tenderness, but involuntary muscular rigidity is never present. Borborygmus, especially in the lower bowel, is usually evident and its presence is confirmed upon auscultation. In those rare instances of true mesenteric adenitis, the enlarged, tender nodes are felt upon deep palpation.

The syndrome is of tremendous importance primarily because of its frequency and secondarily because it must be differentiated from appendicitis. Not only may appendicitis occur in conjunction with upper respiratory infection but in certain cases respiratory infection, per se, appears to be a definite factor in the causation of the acute appendix. Pertinent differential points include the absence of nausea and of muscular rigidity, and the demonstration of excessive intestinal fermentation. Finally, a well executed enema, preferably of sodium bicarbonate (1 level teaspoon to the pint) will usually result in at least temporary relief of the pain.

9. Rheumatic infection is mentioned only to stress the necessity for considering it as a syndrome with multiple, often vague, manifestations such as recurrent epistaxis, sore throats, acute torticollis or "growing pains"—any of which, untreated, are capable of great cardiac damage as the more commonly recognized rheumatic fever and chorea. Since cardiac protection can be afforded only through early diagnosis and prolonged bed rest, it is essential that borderline cases of rheumatic infection be given the benefit of the doubt and treated accordingly.

#### MANAGEMENT.

The management of acute illness in childhood obviously must depend upon the individual case, the underlying condition, etc., but in general certain principles are applicable to the management of most acute infections.

1. Bed rest is often neglected and is seldom overdone. It should be insisted upon with the febrile child and maintained for a variable period after the temperature has become normal. Exceptions are infants under 2 years of age who present no evidence of serious illness and have temperatures of 102 or less. Such cases are often not as restless if confined to a room rather than to bed.

2. Fluid are a very important item in the therapy of acute infections and the ideal route is usually by mouth. Most infants, with judicious urging, will take water fairly well from a bottle, particularly when small amounts are offered at frequent intervals. Liberal dilution of the bottle feeding should not be neglected and offers the double advantage of reducing the ingestion of food and increasing the intake of water. In older children the variety of disguises in which water may be clothed is greater and with some ingenuity large amounts of liquid can be given. Fruit juices, clear broth, carbonated drinks, dilute nectar, weak tea, etc., may be used, depending upon the individual whims of the child. In the presence of nausea, liquid should be chilled. With severe vomiting, nothing is given by mouth for two hours, when teaspoonful amounts are instituted and gradually increased as tolerated.

If a child for any reason cannot take fluid in the usual manner, it may be administered parenterally. The rectal route is of limited use except in older children and intraperitoneal infusions are rightfully on the wane as the procedure is unsound surgically. Hypodermoclysis, especially in infancy, is very effective. In the presence of dyspnea, subcutaneous injection should be limited to the thighs. If more rapid absorption is desired, the intravenous route is indicated, but care should be taken when using glucose not to exceed an isotonic solution (5.5 per cent) or dehydration may result. The exact quantity to be given a child cannot be stated categorically but not more than 10 c.c. per pound and a maximum total of 250 c.c. should be given at one treatment to infants under 2 years of age.

3. Diet obviously should be light and food is not forced under any circumstances. The child's appetite is usually a fairly reliable guide. Milk is not well tolerated in the presence of fever and fats are particularly to be avoided.

4. Bowels are best regulated through the use of enemata, which are also valuable in controlling the fever. Laxatives and cathartics are greatly abused and are seldom necessary. Under no circumstances should calomel or castor oil be administered.

5. Regulation of fever has commonly been accorded undue importance. The conviction is gradually spreading that fever, per se, is not an unmixed evil that necessarily needs combating—that it is, perhaps, a part of the normal mechanism of defense against bacterial invasion. A fever that is not excessive or dangerous in itself rarely demands reduction. Hyperpyrexias of 105 and surely of 106 and over should be reduced both because of the discomfort and restlessness and the danger of a convulsion in the younger child.

To lower fever, hydrotherapy, if carried out intelligently, is quite satisfactory but in unskilled hands the danger of undesirable chilling is very real and in the average case it is perhaps better to use an antipyretic, of which acetylsalicylic acid is the best. While this drug is rightly regarded as a febrifuge, its analgesic and sedative qualities in children are also of great value. The dose is one grain to the year of age, varied as indicated. That it is a nearly harmless drug and has no effect "on the heart" is evident to every observer.

6. Drug therapy. The method of administration justifies brief comment. Most drugs are best given in dry form, the tablet being crushed in a spoon and mixed with a small amount of sugar and water, sweetened orange juice, honey, applesauce or jelly. For the sulfonamides which are often used in relatively large amounts, tomato juice makes an excellent vehicle.

Sedatives demand an important place in pediatric therapy and are often neglected. Phenobarbital has a wide margin of safety and is well tolerated, in amounts approximating one-fourth of a grain, three times a day, to an infant of six months. The prophylactic use of phenobarbital in the acutely febrile child with a sensitive convulsive threshold is particularly worthy of mention. If hypnosis is desired either sodium phenobarbital or seconal in adequate dosage is very satisfactory.

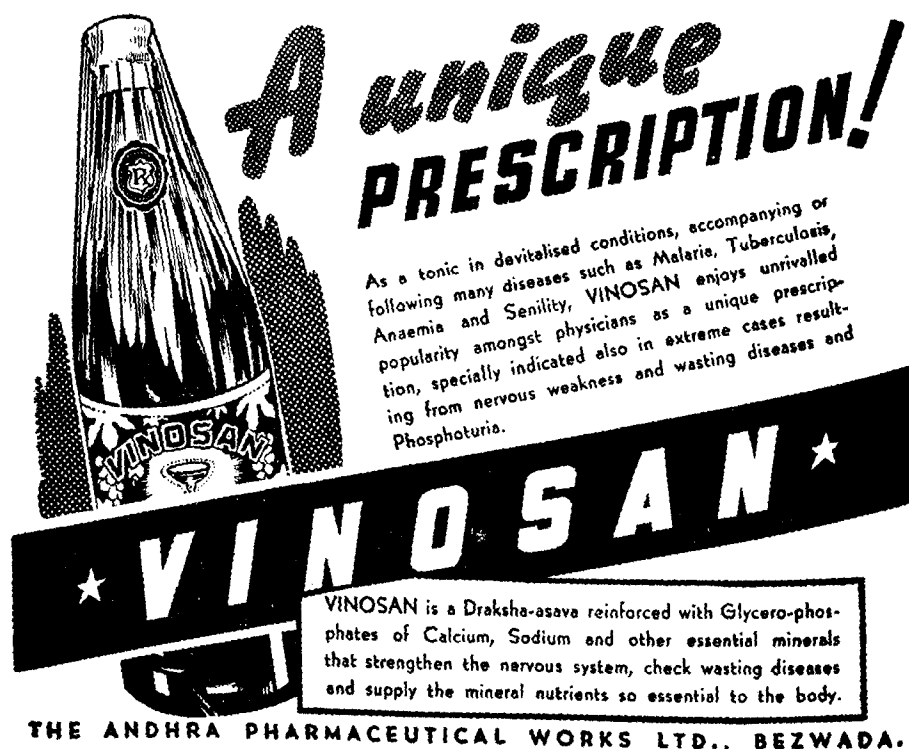
Alkalies have been used extensively for acute infections in recent years on a seemingly rational basis. They occasionally cause gastro-intestinal upset, however, and are not indicated routinely.

While avoidance of harmful drugs is axiomatic, this is particularly true with children. Hot baths, sweats, and diaphoretic drugs so popular among adults as abortive measures at the beginning of a fever have little, if any, usefulness in childhood and may even be harmful unless used with discretion. As previously mentioned, the

initial purge, often drastic, is doubtless a tribute to tradition and seems clearly contra-indicated. The coal tar preparations, especially phenacetin and acetanilid, should be strictly avoided. Amidopyrine is dangerous at any age. Although morphine and atropine are valuable drugs, they must be used initially with great caution in childhood as idiosyncrasy is common and alarming or lethal results may follow. If the sulfonamides are being employed, other drugs should not be used unless necessary.

7. Symptomatic treatment and careful observation for complications require no further comment.

(Rocky Mountain Medical Journal, December 1941.)



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### Extracts.

#### PERFECT SIGHT WITHOUT GLASSES.

By A. SEYMOUR PHILIPS, F.R.C.S.

Assistant Surgeon, Royal Westminster Ophthalmic Hospital.

The attractive slogan has become fairly common. Lately it has bobbed up in the programme of the B.B.C. Brain Trust. Books recommended on the subject are not to be taken seriously as there is very little truth or sense in them. The author's purpose in writing this article is to state what can not be done by eye exercises.

#### WHAT EXERCISES CAN NOT DO

No exercise has been devised which can make a large eye small or a small eye larger, or which can change the shape or refractive index of the eye in any permanent way. Therefore exercises are not a substitute for glasses in long sight, short sight or astigmatism. No exercise will replace glasses which are genuinely needed but unfortunately there are many of us wearing glasses unnecessarily for they are prescribed by practitioners having no medical knowledge. It is not surprising that exercises cure some people of wearing glasses which should not have been prescribed at all.

#### WHAT EXERCISES CAN DO

(a) *Convergence Insufficiency.* To look at any near object requires an effort of convergence and the nearer the object the greater the effort. In people who spend the day on such work it may be that the necessary effort can not be sustained and one eye will then diverge. Binocular vision is thus broken, and diplopia results, which is interpreted by the individual as "blurring of the print." Such cases are not uncommon and for these patients a course of suitable eye exercise is beneficial, and if the general health is sound a cure is likely to result. A holiday may also have the same effect. To complain that the print is blurred is, in some quarters, as much as to ask for a pair of glasses. And another member will then have joined the host of wearers of unnecessary spectacles. Such a person will be a godsend to the cure of bad sight without glasses. A competent oculist would not have given him glasses in the first place, but would have put him on exercises from the start.

(b) *Heterophoria.* In a patient with heterophoria or latent squint the desire for binocular vision keeps the eyes working together, provided the general health is good and the eyes not tired. But when fatigued the eye muscles cannot summon up the effort required to sustain binocular vision, which therefore breaks down and the eyes assume a position of rest, one eye squinting up, down, in or out. The binocular vision breaks down and patient momentarily becomes monocular.

The immediate effect of becoming monocular is to throw out one's judgment of distance, for the amount of convergence required to see an object is a valuable guide to its distance from the observer.

Exercise will help many of these men and to talk to them after such treatment is to get convinced.

—(*British Medical Journal*.)

#### ACUTE CHOLECYSTITIS WITH PERFORATION INTO PERITONEAL CAVITY.

BY C. R. EDWARDS, W. H. GERWIG AND W. L. GUYTON  
BALTIMORE.

Edwards and his associates collected 21 cases from two Baltimore hospitals of gallbladder perforations into the free peritoneal cavity complicating acute cholecystitis. Such perforations cause a diffuse biliary peritonitis which is highly toxic and against which the peritoneum has little resistance. The patients have been under the care of several surgeons. The authors therefore believe that their report is suggestive of the actual percentage of perforations into the peritoneal cavity which might generally be anticipated. During eleven years at the Church Home and Infirmary there were 32,921 admissions, 531 of which were for gallbladder disease and among these there were 96 acute cases with 8 perforations into the peritoneal cavity, or 8.33 per cent. During six years at the University Hospital there were 34,958 admissions, of which 593 were for cholecystitis and among these 98 were acute with 13, or 13.31 per cent. perforations into the peritoneal cavity. With a total percentage of 10.82 this serious complication cannot be regarded as rare. It is generally conceded that patients with chronic cholecystitis may have their operation deferred while being thoroughly studied and prepared, but this policy cannot be applied safely to the acute instances. This is clearly illustrated by the fact that operation was possible for only 6 of the 8 patients from the Church Home; the length of their illness prior to admission was short. The other patients were practically moribund on admission; they failed to respond to treatment and died from the overwhelming infection and toxemia. Twelve of the 13 patients of the University Hospital group were operated on. The remaining patient, ill less than twenty-four hours before admission, was not able to endure an operation. She failed to respond to treatment and died within eighteen hours of admission. There was 1 death among the Church Home group and 2 among the University Hospital group of patients. Bacteriologically, nothing new or unexpected has been observed among these 21 patients. The colon bacillus was recovered from the gallbladder of 6, *Streptococcus faecalis* from 1, *Streptococcus nonhaemolyticus* from 1 and *Staphylococcus aureus* from 1; no growth was recorded

from 4 and no culture was made of the remaining 8. No attempts were made to find any pancreatic enzymes; while the regurgitation of pancreatic and duodenal juices into the gallbladder is possible under some circumstances, it is inconceivable, in view of the pathologic changes encountered in the biliary system of the patients considered. The leukocyte count averaged from 18,000 to 20,000. Other laboratory tests were of no value in determining the severity of the infection. Febrile reactions and pulse rates were variable. Roentgenograms played no part in arriving at a diagnosis. The history and physical examination were so suggestive of gallbladder disease that they have been depended on without roentgenograms. The exquisite tenderness on the slightest pressure over the gallbladder area indicates peritoneal irritation, and if present over the entire abdomen it suggests a rapidly spreading biliary peritonitis. If after the administration of dextrose and salt solution intravenously the patient looks and feels better but shows little or no improvement on palpation, an immediate operation is indicated. In the present series there were ten cholecystectomies, seven cholecystostomies and one partial resection of the gallbladder.

(*Annals of Surgery*.)

#### TREATMENT OF CHRONIC INTESTINAL AMOEBIASIS USE AND ABUSE OF EMETINE.

BY SIR R. N. CHOPRA, C.I.E., M.A., M.D., SC.D. (CANTAB.),  
F.R.C.P. (LOND.) COL. I.M.S. (RETD.) AND I. C. CHOPRA,  
M.R.C.S., D.T.M.

*From the School of Tropical Medicine, Calcutta.*

Emetine injections are by far the most satisfactory immediate line of treatment of an acute attack of amoebic dysentery, but they are generally a failure in the treatment of chronic intestinal amoebiasis and the carrier condition. This present paper is based on 1195 cases of intestinal amoebiasis treated by the Senior author in the Carmichael Hospital for Tropical Diseases.

*Why is emetine effective in acute amoebic infection and not in the Chronic form?* In acute amoebic infection, the amoebae are numerous and in full activity, and are amenable to the action of emetine. The reason is that the gut in this condition is in a hyperaemic state and emetine given in the form of injections quickly reaches the amoebae, which lie in the ulcers, through the blood stream and destroys them. But in the majority of cases, the infection is often not eradicated. Injections especially of inadequate doses, may produce emetine resistant forms; this fact is often not appreciated and one often sees cases which have had injections of  $\frac{1}{4}$  or  $\frac{1}{2}$  grain daily instead of effective doses of one grain.

In relapsing and chronic types of dysentery and especially in long standing cases, fibrosis of the ulcerated area is set up and the capillaries are cut off, thus preventing the access to the parasite of emetine circulating in the blood. The second factor is the infection of the ulcers with intestinal bacteria which lead to chronicity of the lesions. Further, with such added infection, the reaction of the gut becomes markedly acid and as emetine acts best in an alkaline environment, its action is hindered.

If energetic treatment is not started in the early stages of an acute infection before extensive destruction of tissues has taken place, relapses are almost certain to occur. Such symptoms as tenderness on pressure over the colon, localised abdominal pain and thickening are frequently found. The liver is enlarged and tender when hepatitis is present.

*Treatment of relapsing and chronic forms of amoebiasis.* Our aim should be not only the relief of symptoms but also the sterilization of carriers, symptom free or otherwise. The usual procedure adopted is as follows :—

The patient is put on a low-residue diet and a proper course of one of the amoebicidal drugs (Carbarsone, Yatren, or Kurchi alkaloids) is prescribed. This is followed by liquid extract of kurchi in doses of 1 to 2 drs. twice daily after meals for a period of 2 to 3 months. In cases where added infection with the dysenteric group of bacteria is present, a ten days' course of lactose in doses of 3-4 heaped teaspoonfuls in a tumbler of water first thing in the morning is prescribed; lactic acid organism in form of dahi (curdled milk) or tablets of lacteol are given at the same time. In this way intestinal flora is changed. If much mucus is present such drugs such as isapgul are given. If frequent examinations of stools show cystic forms, courses of amoebicidal drugs are repeated. The treatment may have to be continued for many months together.

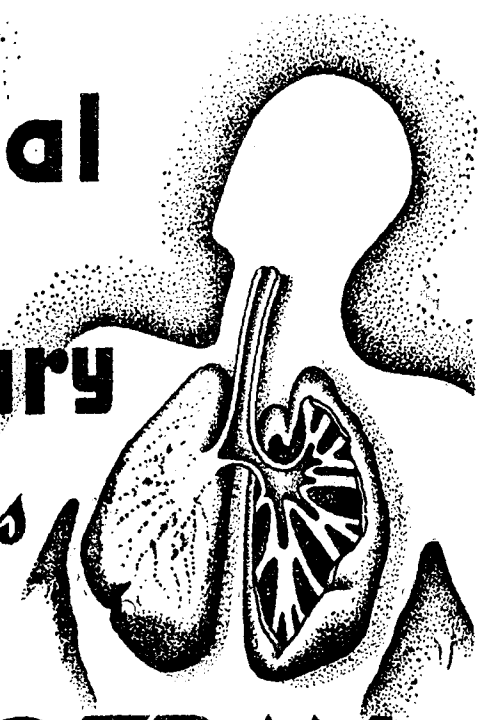
Five groups of drugs are available in the treatment of chronic amoebiasis.

1. *Emetine and emetine-bismuth iodide.* Emetine injections do not cure chronic amoebic dysentery. Emetine by the mouth in form of emetine-bismuth iodide is more effective, as it is absorbed from the gut and reaches the lesions by the capillaries; at the same time a sufficient concentration is maintained in the gut for direct action on the parasite present in the ulcers and free in the lumen. The usual course is 2 grains a day for ten days. The drug is administered in hard gelatine capsules at night before going to bed, three hours after a meal. Luminal 1 gr. or Tincture opii 5 to 7 Min. may be given to enable the drug to be retained. Emetine injections are specific in amoebic hepatitis with or without abscess formation.

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- (4) Diodoquin (64 per cent. Iodine).

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3. *Organic arsenicals.* These consist of stovarsol and carbarsone. Stovarsol is somewhat toxic. Carbarsone in doses of 0.25 gm. twice daily for 15 to 20 consecutive days has proved effective and no toxic effects have been observed.

4. *Kurchi alkaloids.* They have been shown to be effective in the treatment of both acute and chronic forms of intestinal amoebiasis. Kurchi bismuth iodide in doses of 10 grains twice daily has given very satisfactory results. Kurchi is non-toxic and can be given in large doses for prolonged periods. A liquid alcoholic extract of Kurchi in doses of 1 to 2 drs. two or three times a day continued for 2 to 3 months is effective in cases of long standing.

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(*Indian Medical Gazette.*)

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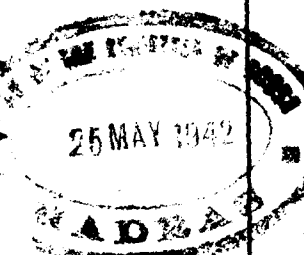
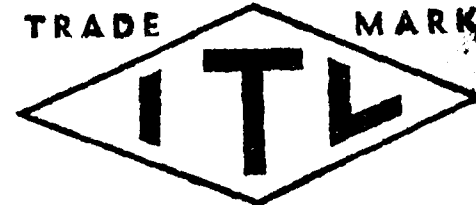
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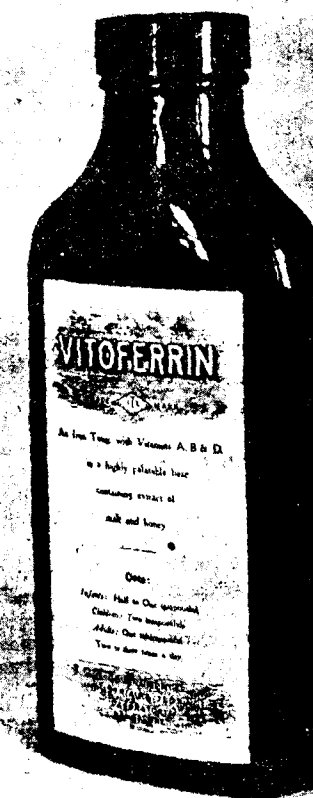
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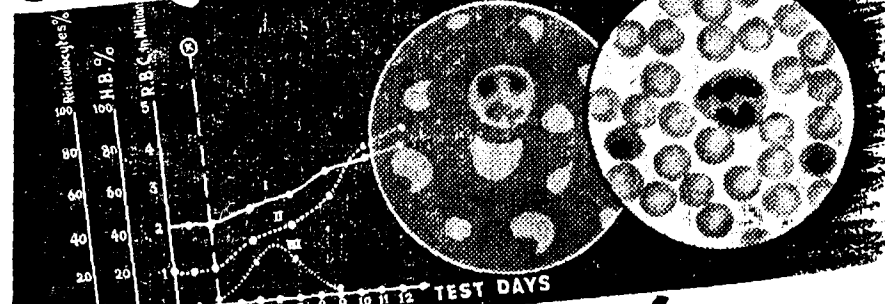
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### DIARRHEA IN INFANTS.

Read by Dr. S. M. Ahmed, M. B., B. S., on 5-8-1941 at the meeting of the I.M.A. Muzafferpur Branch.)

Diarrhea in infants may be classified as follows:—

1. Acute infantile diarrhoea.
2. Dysentery.
  - (a) Amoebic dysentery.
  - (b) Bacillary dysentery.
  - (c) Flagellate dysentery. (Trichomonas, Chilo mastix Lamblia.)
  - (d) Ciliate dysentery (Blantidium coli)
3. Chronic ulcerative colitis.
4. Steatorrhea or Celiac disease.

To-day I shall try to deal on some important aspects of acute infantile diarrhoea.

Three decades ago diseases accompanied by severe diarrhoeas caused almost as many deaths in infants as all other causes combined. Although recent years have seen a marked diminution of the death rate from Diarrhea, yet it is still the largest cause of death in the first year of life of those infants who live beyond the new born period.

The decline in the mortality from Diarrhea has not been due to any single hygienic or prophylactic measure; it has not followed the discovery of some startling new remedy or method of treatment; nor has any fundamentally new etiological agent been discovered. Nevertheless the knowledge in all these fields have been greatly widened. Such simple procedures as prevention of under-nutrition, prompt attention to slight gastro-intestinal upsets and careful guarding of infants' food from bacterial contamination were probably responsible for the prevention of Diarrhea diseases and the changed out-look of those which do occur. But in India the condition is practically the same as was three decades ago in European countries and America. The causes being the absence of mass education and adequate medical aid and public health measures in the villages and most of the towns.

Strictly, Diarrhoea is the presenting symptom of a number of disorders which are etiologically unrelated. However the pathogenesis of the symptom is much the same and the symptomatic treatment is almost identical. Despite etiological diversity, the symptomatic and physiological similarity of the disturbances make it rational to group diseases in which diarrhea is the presenting symptom in one category.

*Etiology.*—The causes of Diarrhoea are, for the most part obscure. As far as one can judge, at present, attacks of Diarrhoea are brought about by several factors.

- (1) Age. (2) Under nutrition. (3) Defects of Digestion. (4) Dehydration. (5) Infections. (6) Seasonal incidence.

1. *Age.*—Infants are especially prone to develop Diarrhoea, and in general, the younger the infant the greater the tendency. However the greatest mortality occurs at about the third month of life.

2. *Under-Nutrition.*—Next to age under nutrition is the greatest predisposing cause of Diarrhoea. Not only do under nourished babies develop Diarrhoea more often but they also show more severe symptoms. Under-nutrition can be brought about in a number of ways which may be classified as follows:—

(a) Qualitatively deficient food with adequate calories, examples or deficiencies of protein, carbohydrate or vitamin.

(b) Quantitatively insufficient intake of an otherwise suitable food

(c) Defective digestion, Celiac disease, Pancreatic insufficiency.

(d) Constitutional inadequacy.

3. *Defects of digestion.*—Celiac disease, and pancreatic insufficiency are the true digestion defects in children.

4. *Dehydration.*—Infants may develop fever, diarrhoea and vomiting if the intake of water is limited so as to produce slight dehydration. If dehydration is marked even water may produce vomiting. Concentrated protein foods are most effective means of producing diarrhoea, and vomiting in the presence of slight dehydration. Such facts suggest that, when hot weather produces slight dehydration, food may precipitate diarrhoea. Apparently fever may have a similar effect. Further more, diarrhoea produces dehydration and sets up a vicious cycle whereby food aggravates diarrhoea, vomiting and dehydration.

5. *Infection.*—In general, outside of the infection with dysentery bacilli no external infection has been established as a cause of diarrhoea. Dysenteric infections often give rise to early symptoms identical with those characteristic of the etiologically non-specific group of diarrhoeas. However, the presence of blood, mucus and pus in the stools usually identifies specific enteritides. Nevertheless,

it seems likely that other bacterial causes of diarrhoea will be demonstrated.

6. *Seasonal incidences.*—Diarrhoea is apt to appear more frequently in September or October, otherwise the incidence is fairly uniform throughout the year.

Finally it should be pointed out that severe diarrhoea seems to result from a combination of several possible causes. The soil is prepared by under-nutrition particularly in young babies, the seed is planted in the form of infection or irritating food, fever, hot weather and lack of water are environmental factors which favour the growth of the diseases.

*Pathological Anatomy.*—The tissue are dry. Blood shows, characteristic of dehydration. The intestines may be distended. The liver is apt to be loaded with fat. Terminal pneumonia is frequent.

*Signs and Symptoms.*—For practical purposes we may divide the consideration of signs and symptoms into two heads:—

(1) Diarrhoea without grave constitutional symptoms.

(2) Diarrhoea with grave constitutional symptoms

1. *Diarrhoea without grave constitutional symptoms.*—Mild cases are common than the severe ones, but there is no sharp line of demarcation between the two groups and slight aggravation of any of the symptoms of the mild cases will convert them into severe ones.

(1) *Stools:*—Five to six loose stools a day without constitutional symptoms, stools are not watery; colour may be slightly greenish.

(2) Colour of the skin is rosy.

(3) There is no change in the disposition of the child.

(4) There is no fever.

(5) The child continues to gain in weight, or at least the weight is stationary.

*Treatment.* The treatment is largely expectant. An adequate diet is required so that undernutrition does not develop. The babies should be observed closely so that constitutional symptoms may not be overlooked. The sugar content in the foods should not be reduced, but fat content should be reduced to about 2 per cent.

A useful prescription at this stage is, to give the child:—

1. Hydrarg cum crete, Pulv Ipecac radi, Lactopeptine, Pancreatin, Creta preparata.

Thrice daily, dose according to age.

#### DIARRHEA WITH CONSTITUTIONAL SYMPTOMS.

Onset sudden, occasionally benign diarrhea changes into severe type.

*Stools.*—Watery, yellowish to bright green and contains mucus. Number 10 to 20 a day Stools irritating in character and produce excoriation of the buttocks.

*Weight.*—With increase in the number of stool and its water content, loss of weight occurs.

*Skin.*—Loses its rosy colour, becomes pale, ashen gray and seems to lose some of its translucency; if it is lifted up in a fold, it returns more slowly to the normal contour than normally. The cheeks appear drawn, and the eyes are surrounded by drall circles, the fontanel may be sunken. The musculature loses tone, and becomes flabby. The abdomen is normally flat and often scaphoid. Distention occasionally occurs and it is a bad sign.

*Disposition.*—Changes; he is no longer interested in the surroundings. Sometimes there is apathy, sometimes restless excitement. The cry is shrill and sharp. Coma and convulsion may occur. Vomiting, regurgitation of food and loss of appetite are almost invariably present.

*Fever.*—Usually present 100 to 104 degrees.

*Urine.*—It is concentrated and may contain Albumin, leucocytes and granular casts. Anuria occurs in severe cases.

*Breathing.*—It may be rapid (35 to 40) and deep. Sometimes very rapid 60 or more per minute and deep. Terminally vomit and stool may contain blood and acute intestinal distention is a terminal sign. Sign of circulatory collapse occurs in severe cases, the lips and extremities may become cyanosed, the pulse is rapid and heart sounds feeble. The extremities feel cold, though the rectal temperature is high. Some patients show a pulse rate slower than normal and such cases are usually fatal.

*Treatment.*—The treatment is symptomatic or it may be called physiological as it aims to correct the physiological disturbances. The treatment is aimed at:—

- (1) Stopping further loss of water and Electrolyte.
- (2) Restoration of Interstitial fluid.
- (3) Treating the infective process if found out.

1. *Stopping further loss of water and Electrolyte.*—Administration of all food and water by mouth should cease as in a dehydrated infant food and even water may induce vomiting and aggravate diarrhoea. Starvation should be carried on until the character of stool indicates that considerable reabsorption of intestinal juices is taking place. As long as the stools are watery and leave little but a stain on the linen, this is not the case. The persistence of green colour should make one cautious in resuming the feeding but if little water is present in the stool, food may sometimes be given, before the stools become brown or yellowish. With the improvement in character of the stool, certain toxic symptoms should abate. Fever should diminish or disappear. The weight becomes stabilised. The skin improves and mental state is more nearly normal. The period of starvation is usually one day but may be more than four days and recovery has occurred in cases in which no food was given for eleven days.

2. *Restoration of interstitial fluids.*—The Chief method of correcting dehydration is the subcutaneous administration of solution containing sodium chloride. Subcutaneous saline should be administered immediately and repeated as long as dehydration persists or watery stools are evacuated. The best guide as to amounts and frequency for the administration of subcutaneous saline is the urine. Sufficient solution should be given to induce a diuresis other guides are skin turgor and weight. A dehydrated infant should receive enough subcutaneous saline so that in twenty-four hours the skin turgor returns to normal and a gain in weight takes place or at least no further loss in weight occurs.

About half an hour after the saline, an infusion of glucose solution (10 to 20 c. c. per Kilogram of body weight of 10 per cent. solution) should be given intravenously and in general should be continued once or twice daily.

3. *As no specific infective cause has yet been definitely found out, no specific line of treatment can be mentioned here. Any infective process in the infant should be promptly dealt with. Intestinal bacteriophage administered every three hours with plain water by mouth has proved of marked value in many cases.*

*Resumption of feeding.*—Food is started when the consistency of the stools indicates resumption of the function of reabsorption by the intestines and when toxic symptoms have diminished.

*Contra indication.*—(1) Diminished skin turgor (2) Greyish pallor (3) Nausea or vomiting (4) Distention (5) Watery stools (6) Fever. As long as these contraindications do not disappear or at least normally abate no food should be given.

In resuming feeding, the safest procedure is to offer small feeding every two, three or four hours. If no aggravation of symptoms occur, the amount of food is increased.

The old argument as to what is the best type of food for a baby with diarrhoea is becoming less important as it is realised that when a baby is ready to take on milk mixture he is probably ready to take almost any of the well recognised feedings. The total intake is more important than the type of food. When a tendency to vomiting is present, feedings low in fat are probably a little better tolerated.

## TUBERCULOSIS\*

BY RUSTOM J. VAKIL, M.D., M.R.C.P., D.T.M.

*Honorary Assistant Physician, K.E.M. Hospital, Bombay.*

The problem of tuberculosis is much too vast to tackle in the space of an hour or so. Literally, hundreds of books have been written on the subject and when we consider the deficiencies in our knowledge of tuberculosis at the present day, it looks as if the future generations of medics will be burdened by several hundred more books on tuberculosis.

The importance and high incidence of tuberculosis are not sufficiently appreciated either by the medical profession or by the laity. Pulmonary or lung tuberculosis has been rightly described as "the commonest, most fatal and perhaps, the saddest of those diseases which oppress mankind." In the words of Osler, "it transcends all other maladies in the total number of its victims and the cost to society in civilised countries."

To give you an idea of its frequency, let me quote a few figures. In 1910 it was computed that one-seventh of all deaths are due to tuberculosis. Since the death-rate from this disease has been steadily declining for the last forty years or so, we can say that at the present-day tuberculosis accounts for one-tenth to one-twelfth of all deaths. Reinhart found on examination of 360 human bodies that as many as 96.38 per cent. had tuberculous lesions or deposits. It 63.9 per cent. these lesions had healed. It looks as if practically every one of us gets infected with tuberculosis at some period of his or her life, usually in early childhood. Fortunately, in the majority of cases the lesion heals or disappears.

In civilised countries, an enormous amount of money is spent annually on the prevention and treatment of tuberculosis. Fisher calculated the net cost for a tuberculous patient in America as 4,000 dollars. Since the death-rate in that country in 1906 was 138,000, Fisher calculated the annual expenditure on tuberculosis at about 1,100 million dollars.

Pulmonary tuberculosis has been known to man from very remote times. It was familiar to all the great civilizations of the past. There are records of it on Babylonian tablets. Tuberculous diseases of the spine has been observed in Egyptian mummies.

Hippocrates, "the father of medicine," who lived from 460 B.C. to 376 B.C., gave an excellent description of tuberculosis; his description of the disease remained unparalleled for centuries. Aristotle, a contemporary of Hippocrates also alluded to the disease tuberculosis. Even in the days of the ancients the importance of open air and sunlight in the treatment of tuberculosis was realized.

\* A lecture delivered before the St. Xavier's College, Science Society.

Aretæus in 50 A.D. noted the beneficial effects of sea-voyages and country air in the treatment of this disease. Pliny believed in the healing powers of pine forests.

In 1868, Villemin wrote exhaustively on the epidemiology of tuberculosis and for the first time found it possible to transmit the disease to animals. In 1882, Robert Koch demonstrated the causative organism of tuberculosis for the first time in various tuberculous lesions of the body. Since that time, little has been added to our knowledge of tuberculosis except perhaps in the field of therapeutics. It is a point of historical interest to know that Koch stained the bacillus with methylene blue rendered faintly alkaline with caustic potash and used vesuvin as a contrast agent. It was left to Ziehl and Nielson in later years to devise much more efficient staining method for the tubercle bacillus.

There are certain interesting features about the distribution (geographical and racial) of the disease tuberculosis, which deserve mention.

Tuberculosis occurs at all latitudes and altitudes and in all climates. It is rare in Alpine and Arctic regions, in Mexico, Colorado etc. It occurs most frequently in low-lying districts with temperate climates. Different races differ considerably in their susceptibility to infection. Some races are more susceptible than others. In North America, for example, the Negroes suffer much more severely from tuberculosis than the white population. In 1920, the death-rate from tuberculosis in the whites was about 1 per 1000, while in the Negroes it was about 3 to 4 per 1000. Jews are said to exhibit a high degree of resistance to tuberculous infection.

In primitive, aboriginal and uncivilized races, tuberculosis is absent or rare, not from an inherent immunity in the population but from lack of opportunity to infection. Once the disease is imported to these tubercle-free districts, usually by Europeans, the disease flares up and literally destroys the major part of the population. To cite an actual instance: Tuberculosis was unknown amongst the North American Indians. With the advent of Europeans and civilization, the disease flared up with such violence in the native population that incidence of tuberculosis in 1896 was 150 per 1000 individuals, while the death-rate was 30 per 1000. Not only do these primitive races acquire the disease more easily, once it is introduced into the community, but they exhibit a different type of disease—a more virulent and fulminating form of disease altogether.

One or two features about the death-rate of tuberculosis have caused a lot of controversy in medical circles. Why, for instance, has the mortality rate from tuberculosis been steadily declining during the last sixty years or so in all civilized countries? It is true that this decline is partly accounted for by better care in hygiene and sanitation and by the institution of tuberculosis sanatoria. But

there must be other factors as well, for the decline in mortality started twenty years before the discovery of the bacillus by Koch and about 40 years before the advent of sanatoria. In England and Wales, the mortality rate has declined by 72 per cent. since 1851-1860, the present death rate being about 37,000 per annum.

The age mortality from tuberculosis is interesting. During the first year of life (*i.e.* in infancy), the mortality rate is extremely high; though believed to be 100 per cent. at one time, the actual rate during infancy is 70 per cent. (Hamburger). After the second year of life, there is a decline a low point being reached between the ages of 10 and 15. After the age of 15, the death-rate rises steadily and attains a peak between 30 and 40. After 40 there is another decline.

#### PREDISPOSING FACTORS.

Certain factors are capable of increasing or decreasing (as the case may be), the susceptibility of the individual to tuberculous infection. We have already considered the question of racial predisposition. The general condition of health of the patient plays a part. An individual debilitated by disease, ill-health or poverty is much more likely to get affected than a normal healthy individual. Overcrowding and insanitation also predispose to tuberculosis. Dusty occupations often predispose to tuberculosis. This is so in the case of stone-masons, tinminers, emery grinders and file-makers. In the case of coal-miners and Portland cement workers the reverse holds true; these individuals are less prone to tuberculosis than even normal individuals. Many different theories have been put forward to explain the resistance of coalminers to tuberculous infection.

#### BACTERIOLOGY OF TUBERCULOSIS.

The cause of tuberculosis, as shown by Robert Koch in 1882, is the tubercle bacillus, sometimes known as Koch's bacillus.

The tubercle bacillus is usually assigned to the genus *Mycobacterium*. The characteristic features displayed by members of this genus are: the bacilli are slender rods which stain with difficulty, are acid-fast, non-motile, non-sporing, aerobic, slow-growing and gram-positive. Clubbed and filamentous forms are frequently observed.

The question has often been raised, whether the causative organism of tuberculosis is a bacillus or a fungus? The tubercle bacillus takes so many diverse forms that some bacteriologists have regarded it as a parasitic fungus rather than a bacillus. Some bacteriologists put the tubercle bacillus in an intermediate class between bacteria and fungi. Hence the terms, "Tuberculomyces" (Coppen Jones) and "Mycobacterium tuberculosis" (Marpmann) used for the tubercle bacillus.

The tubercle bacillus belongs to the important group of "acid-fast bacilli." These are so called because of their ability to withstand the decolourizing effect of mineral acids after being stained

This power to hold or retain aniline dyes in spite of prolonged exposures to acids (alcohol in some cases) is known as "acid-fastness" or "acid-resistance" (acid-alcohol resistance in some cases). It serves to distinguish this group of bacteria from most other bacteria.

The degree to which acid-fastness is displayed varies with the different members of this group; even in a given organism the degree of acid-fastness is not constant and may be affected by extraneous factors.

The main members of this group are:—

- (1) The tubercle bacillus or *myc. tuberculosis*.
- (2) *B. Lepre*. This was the first member of the acid-fast group to be discovered. It was isolated from leprosy cases by Hansen in 1874.
- (3) *Johne's Bacillus*, isolated in 1895 by Johnne and Frothingham, is responsible for an intestinal disease of cattle known as *Johne's disease*.

The above are examples of pathogenic acid-fast bacilli. There are however many saprophytic members which are widely distributed and frequently encountered *viz.*:—

- (4) *Smegma bacillus*.
- (5) *Butter bacillus* or *Myc. butyricum*, isolated by Rabinowitch.
- (6) *Timothy-grass bacillus* or *Myc. phlei* found in timothy-grass and in dust.
- (7) *The Mist Bacillus* or *My. Stercussis*, first isolated from a dung-heap by Moeller in 1901 and later found in the excreta of donkeys, cows and herbivora. (The German word *Mist* means manure.)

*Cause of acid-fastness.*—(1) The property of acid-fastness is usually attributed to the presence of large amounts of an unsaponifiable wax in the structure of the acid-fast group of bacilli. The pathogenic members have more waxy material than the saprophytic members, the maximum amount being present in the tubercle bacillus. (2) Sordelli & Arena, on the other hand, attribute acid-fastness to the presence of a semipermeable membrane around the bacillus.

*Morphology.*—The tubercle bacillus is a minute, colourless rod, straight or with a slightly bent shape, variable in length and slightly in thickness. The ends are rounded. The length varies from 1.2 to 4  $\mu$  while the thickness averages about 0.4  $\mu$ . The bacilli occur singly or in small clumps; occasionally, the Chinese letter arrangement of the *Diphtheria bacillus* is faked. They tend to be longer and thinner in the animal body than in culture. Anomalous forms are frequently encountered. Clubbed forms, branched forms and long filamentous forms have all been described.

Kahn describes a developmental life cycle for the tubercle bacillus. According to him, the bacillus does not multiply solely by

simple fission but displays a highly complex form of reproduction. The rod first becomes segmented into diplococcal form; next appear granules from these forms. From these granules, tiny rods sprout and develop. It is possible that the above-mentioned granules correspond to the "grauclles" described by Much in chronic tuberculous lesions. Is there a filtrable form of tubercle bacillus? This question has come into prominence of late. In 1910 Fontes filtered a dilution of tuberculous pus through a Berkefeld filter and injected the filtrate into guinea-pigs. Two weeks later, one of the animals developed enlargement of groin-glands. An extract of the spleen from this animal was inoculated into fresh guinea-pigs. The latter showed acid-fast bacilli in the glands and lungs after some time. This experiment has been successfully repeated by others. It has therefore been suggested that the tubercle bacillus assumes a minute form, capable of traversing filters. The above experiment is not conclusive, since it is possible for a few bacilli to go through the pores of a filter; also acid-fast bacilli have been demonstrated in the glands of perfectly normal guinea-pigs. French clinicians have described a form of tuberculous meningitis where tubercle bacilli cannot be demonstrated in the spinal fluid. They attribute the condition to a "virus tuberculeux."

*Types of Tubercle Bacilli.*—Four main types of tubercle bacilli are recognised. (1) Human, (2) Bovine (These two are mammalian types), (3) Avian, (4) Piscene or "cold-blooded". The mammalian types affect man and mammals but not birds or reptiles. The avian form affects birds and occasionally rabbits and pigs. Some continental authorities have claimed the occasional occurrence of an avian form of tuberculosis in man. This opinion is not shared by British authorities. The cold-blooded type of tubercle bacillus only affects fish and cold-blooded animals.

The possibility of mutation of the tubercle bacillus from one type to another has been suggested on inconclusive evidence. The general present-day opinion is that the different type of tubercle bacilli are not interchangeable. The so-called "intermediate forms" are probably variants of one or other type of tubercle bacillus.

The bovine type of tubercle bacillus is a frequent cause of tuberculosis in man, especially in children. The great majority of cases of pulmonary tuberculosis (over 90 per cent at any rate) in man are due to the human type, while about half the cases of glandular and intestinal tuberculosis have been claimed as being of bovine origin.

*Staining Methods.*—The method of staining usually employed for the tubercle bacillus is the Ziehl-Neelsen method of staining. Ziehl was the first to suggest the use of carbol-fuchsin while Neelsen was responsible for increasing the strength of carbolic acid in the stain. The Ziehl-Neelsen stain contains basic fuchsin (1 part), absolute alcohol (10 parts) and a 5 per cent aqueous solution of phenol

(100 parts). Heating is essential for 5 to 15 minutes as it allows the aqueous dye to penetrate the waxy envelope of the bacillus. The phenol in the stain acts as a mordant. 15 to 20 per cent. acid is used after staining. Counter staining is done with 1 per cent. methylene blue for 5 minutes or alternatively with 1 per cent picric acid, the latter giving a yellow background. It is said that 100,000 bacilli must be present per c.c. before they can be detected by this method.

*Cultural Reactions.*—Different types of tubercle bacilli grows readily on culture. The cold blooded type grows readily on ordinary media while the mammalian types are extremely difficult to grow; the avian type occupies an intermediate place.

Factors essential for growth are:—

- (1) Presence of air. The bacilli will not grow under strictly anaerobic conditions.
- (2) Presence of moisture. Hence the use of a paraffinised plug on the mouth of culture tubes to prevent evaporation of water.
- (3) Reaction of medium from pH 7.0 to pH 7.6.
- (4) Optimum temperature. For human and bovine types it is 37° C, for the avian type 40° C and for the cold blooded type 25° C.

Media most in use are:

- (1) Dorsett's egg medium.
- (2) Glycerin-agar or broth.
- (3) Glycerine potato medium.
- (4) Corper's medium. (Potato with crystal violet.)
- (5) Jensen's modification of Lowenstein's medium gives a good growth. Contaminated material is mixed with 4 per cent. NaOH or 6 per cent. HSO and allowed to stand for 15 to 20 minutes; the mixture is centrifuged and the sediment rendered neutral to litmus and seeded on slopes of Lowenstein's medium. A good growth is obtained within 2 or 3 weeks.

*Nature of Growth.*—On Dorsetts' egg, dry friable colonies with a wrinkled surface are obtained in 4 to 6 weeks. With Jensen's modification of Lowenstein's medium a good growth is obtained in 2 to 3 weeks. The human type gives large, rough, bright, orange-yellow colonies while the bovine type gives small smooth, discrete and colourless colonies.

*Chemical structure of the Tubercle Bacillus.*—This important subject has been recently made subject of study at the Yale University by Anderson and his colleagues. Much knowledge has been gained through their studies. The tubercle bacillus is made up of three main constituents viz. (1) Lipoids. These are of 3 main types: (i) Phosphatides or phospholipids, which give on hydrolysis several

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in the saprophytic members; the actual order being; Human > Avian  
> Bovine > Saprophytes. With polysaccharides, the order is revers-  
ed. The phosphated and protein fractions are antigenic; polysac-  
charides do not call forth antibody formation. The protein represent  
the active constituent of tuberculin.

*Pathogenicity to Animals.*—Tuberculosis is not observed in all  
animals. A difference is noted depending on whether animals are  
in the natural and wild state or are domesticated. Tuberculosis is  
practically absent in animals and birds in the wild state. Domesti-  
cated animals and birds are liable to the disease; this is especially so  
with dairy cattle. In America 10 to 15 per cent of dairy cattle have  
tuberculosis, in the British Isles and Europe, percentages of 30 to 70  
per cent have been reported as being tuberculin positive. Cattle  
tuberculosis is practically unknown on the Isles of Jersey and  
Guernesey.

In zoological gardens, tuberculosis has been observed in monkeys,  
apes, rabbits, guinea-pigs, and antelopes, zebras, lions, tigers, foxen,  
elephants and giraffes.

Both human and bovine types of tubercle bacillus are capable of  
inducing fatal and progressive tuberculosis in guinea-pigs, even in  
minute doses Rabbits, goats, cats and calves though susceptible to the  
bovine type are unaffected by the human type of bacillus.

*The Guinea-Pig Test.*—This is a sensitive method, in great use,  
for the detection of tuberculosis. It is said to be 1000 times more  
sensitive than the Ziehl-Neelsen method of detection.

In the guinea-pig test, a suspension of contaminated material  
is injected into the thighs of two guinea-pigs, intramuscularly or  
subcutaneously. Since the latter route is prone to give ulceration,  
the intramuscular route is preferred. The two guinea-pigs are killed  
after 3 week and 5 or 6 weeks respectively. Even if the infection is  
missed in the first guinea-pig, it will be obvious in the second.  
Feldman's modification of the guinea-pig test, where the material is  
injected into the brain of the guinea-pig is said to give a more rapid  
result.

*The Miliary Tubercle.*—This may be described as the "unit of  
tuberculosis".

Tuberculosis is usually classified with leprosy, syphilis, and  
actinomycosis as granulomata. The characteristics of granuloma  
are the localized response of the tissues to the infection and the  
formation of nodules surrounded by granulation tissue.

Each tubercle is made up of several layers of cells, the main  
constituents being :—

(1) Epithelioid or endothelioid cells. These cells are the first to appear. Their characteristic feature is the vesicular or sac like appearance of the nucleus. These cells are derived from the reticulo-endothelial system of cells.

(2) Giant cells of tuberculosis. These are sometimes known as the "foreign body type of giant cells". They are quite different from the Dorothy Reed cells of lymphadenoma and from the leproid cells of leprosy. There may be as many as 80 or even 100 nuclei in one giant-cell, arranged peripherally, usually in the form of a horse-shoe. The giant cell is said to arise from endothelioid cells either by fusion of cells or by intracellular division of nuclei. The giant-cell performs the function of a scavenger cell.

(3) Lymphocytic cells or small round cells. These arise from neighbouring lymphoid tissue masses. Their function is unknown.

(4) Fibroblasts and fibrocytes. The former possess nuclei.

*Caseation.*—The central part of a tubercle undergoes a form of degeneration known as caseation. The cheesy material formed is known as caseous matter. Caseation is due to two factors:—

(1) The avascular nature of the tubercle. The blood supply of tubercles is very poor.

(2) Due to the toxic action of tubercle bacilli. In rare cases, tubercles may actually undergo resolution and disappear but in the great majority of cases they either calcify or spread.

*Immunological Problems.*—Immunity has been defined by Rich & McCordock as a "relative resistance of the body to living tubercle bacilli." Allergy is different. Here the infected body is altered in such a manner that it reacts violently to the relatively bland protein of the tubercle bacillus.

*The Koch Phenomenon*—It has been experimentally demonstrated that when a dose of tubercle bacilli of moderate virulence be inoculated into the skin of a susceptible but healthy animal like the guinea-pig, a "primary lesion" arises. This is tuberculosis in its purest form. A small swelling appears at the site of injection in 10 to 14 days and breaks down. The ulcer does not heal but is progressive. The lymphatic glands are swollen and caseous. If a second injection is given (ten days or more after the first), and indurated area appears at the site of injection and ulcerates. The ulcer heals after some time. The lymph glands are not enlarged.

The difference in the response of animals to primary and secondary infections is known as the Koch phenomenon.

For the secondary infection it is not necessary to inject living bacilli. Even dead tubercle bacilli are capable of provoking the reaction.

A similar phenomenon is observed in man. Primary infection is usually observed in childhood, practically every child being exposed at one time or other to tuberculous surroundings. A small

focus, known as Ghon's focus is observed in the affected lung in any lobe. The hilar glands are enormously swollen and frequently caseous.

Secondary infection represents the adult form of tuberculosis, the individual having been previously infected in childhood. In this type, the initial focus is known as Assmann's focus and is situated in the subapical region of the lung; the hilar glands are not enlarged in this type.

Though the primary type of infection is usually confined to children it may occur even in adult life as in the case of primitive races which have suddenly been subjected to tuberculous influences.

The question of *Re-infection* in tuberculosis frequently crops up. On the basis of the Kitch phenomenon, it was believed for some time that a permanent immunity is established after the primary infection and re-infection cannot occur. In other words, the tuberculosis of adults is due not to a second dose of tubercle bacilli but to a "flare-up" or "lightning" of an old partially healed focus. This view is no longer held, the adult form of tuberculosis being regarded as secondary or re-infection.

*Modes of infection*—If tuberculosis is due to the tubercle bacillus, how does the latter gain entrance to the body. There are several possibilities:—

(1) *Congenital transmission.*—This is most unlikely. The present-day tendency is to regard all cases of tuberculosis as post-natal in origin. It is true that tuberculosis is encountered in early infancy but this may well be post-natal infection from the mother or from tuberculous surroundings.

(2) *By Inoculation.*—Tubercle bacilli may be introduced into the body through the skin, either through abrasions, or secondary to puncture wounds. This form of the disease is usually observed in butchers, in autopsy attendants and in pathologists.

(3) *By Inhalation.*—This is the most likely mode of infection in cases of lung tuberculosis and represents the general consensus of opinion in English-speaking countries. A controversy however exists regarding the exact mode of inhalation of the tubercle bacillus.

Fligge and his followers suggest inhalation of minute dropets of sputum projected from the mouths and noses of open cases of tuberculosis during sneezing coughing and conversation, as the mode of inhalation (droplet infection). During bouts of coughing tubercle bacilli are projected to varying distances, upto a metre and half. Sneezing is the most effective method of projecting bacilli to great distances. To credit this form of infection, the following example is frequently cited. In a small village, there were two practising midwives. One of these midwives was in the habit of blowing into the mouths of new-born babies when practising artificial respiration. She lost 10

babies in 1 year from tuberculous meningitis. The other midwife had not a single case of meningeal infection (Boyd).

Cornet and his school suggest inhalation of infected dust particles as the cause of lung tuberculosis. According to them, droplet infection is unlikely since droplets soon "come down" to earth. When drying of tuberculous sputum occurs, the bacilli are said to "ride" on particles of dust and floating about in the air are inhaled. Cornet on examining 149 specimens of dust from hospitals, public buildings and private tuberculous wards, found tubercle bacilli in 40 specimens.

(4) *By Ingestion.*—In 1904, Von Behring suggested tuberculous infection of the lung through the alimentary tract. This view was subsequently upheld by Calmette and Guérin of the Pasteur Institute in 1905 who supported it with ingenious experiments. Hence this mode of infection is usually credited to the French school. According to this school of thought, the tubercle bacilli take a devious route via the intestinal wall, the mesenteric glands, lymph channels and hilar glands to lung.

(5) *Tonsillar mode of infection.*—There are some workers who suggest infection of the lung apex via the tonsils, tonsillar glands, deep cervical glands, lymph-channels and apical plicura to the lung-apex. This is very unlikely since lymph-channels cannot be demonstrated between the deep cervical glands and the apices of the lungs.

#### PREVENTION OF TUBERCULOSIS.

(1) *Isolation or segregation of "open" cases of tuberculosis.*—This is very difficult to achieve in India. To my mind, this is the most important single measure effective in the prophylaxis of tuberculosis. "Closed cases" need not be isolated as they do not bring up tubercle bacilli in the sputum and are not a danger to the community like the "open cases". I know of a lady, who through neglect on her part, has now both her children affected with lung tuberculosis. It is usually through a false sense of duty or love that relatives and children usually fall prey to the infection.

(2) *Protection or separation of infants and children from tuberculous parents.*—This has been successfully practised in France since 1903 the children being separated from their tuberculous surroundings. This successful and economical method of segregation is known as the *Grancher system*.

(3) *Proper disposal of sputum.*—Indiscriminate spitting in the streets and tenements is, by no means, an unusual sight in this country. When we consider these grave implications and consequences it can be described as little short of a criminal offence. The practice should not only be strongly discouraged, but made a punishable offence. You will appreciate the importance of this fact when you realise that the usual method of infection in lung-tuberculosis is by inhalation of infected sputum.

(4) *Abolition of the purdah system.*—To realise the importance of this factor in the incidence of tuberculosis you have only got to glance at the statistical reports for India. There is a much greater prevalence of lung-tuberculosis in purdah women than in any other section of the community. The high incidence in such cases is probably due to lack of sunlight and fresh air.

(5) *Pasteurization or boiling of milk.*—One must appreciate the degree of heat-resistance displayed by the tubercle bacillus. In perfectly dry conditions, the bacillus can withstand temperatures of even 100° C for 20 minutes. In fluid suspensions and in milk the tubercle bacillus is usually destroyed by a temperature of 60° C within 30 minutes provided a protective surface pellicle is prevented from forming.

This mode of infection is important in children and accounts for a large percentage of cases of bovine tuberculosis. It is said by some authorities that the giving of tuberculous milk to children is not a necessary evil as it probably immunizes them against re-infection in adult life. Such an attitude is dangerous since bovine tuberculosis in childhood is by no means a less serious condition than tuberculosis in adults and death may result. Besides, doses have to be repeated in order to maintain immunity. There is no guarantee that one of these doses will not prove fatal.

(6) *Improvement of hygienic conditions and prevention of overcrowding.*—This matter lies within the domain of the sanitary authorities and the municipality. Overcrowding is usually secondary to poverty and hence is difficult to abolish.

(7) *Education of the public.*—The general principles of hygiene and sanitation should be inculcated into all growing minds and be made the subject of lectures in schools and colleges. Parents should receive this kind of education as well as the children.

(8) *The question of prophylactic vaccination* is a much discussed one. Koch was able to immunize guinea-pigs by giving them tuberculin. Immunization by dead vaccines has been attempted by many workers with varying success. In the opinion of Calmette and several others, dead vaccines are of no use. Calmette introduced a "living vaccine" of an avirulent bovine strain widely known as B.C.G. (Bacille Calmette Guérin). The bovine strain was rendered avirulent by several years of subculturing on glycerol-bile-potato medium. This vaccine has been tried extensively in infants, three doses being given by mouth during the first ten days of life. The results have not so far proved conclusive in either direction.

(9) *Early detection of tuberculosis.*—Attempts have recently been made to detect tuberculosis in its earliest stage, when treatment is of avail and when the likelihood of infecting others is less. In the early stages of the disease there may be no obvious signs or symptoms—(latent tuberculosis). Such a case is obviously dangerous

as it passes unnoticed. Routine x-ray examinations of the chest in apparently normal young people aged 14 to 18, by Wingfield and Macpherson showed evidence of tuberculosis in about 1% of cases. They therefore suggest a routine examination of adolescents for evidence of latent infection.

#### TREATMENT OF PULMONARY TUBERCULOSIS.

(1) The value of *fresh air* has been recognised for ages. It acts as a tonic and makes the individual harder and capable of withstanding adverse influences.

(2) *Change of climate.* In the days of the Romans, Egypt was regarded as the ideal place for consumptives. In the opinion of some authorities this improvement was due not to the climatic conditions of Egypt but to the nausea and vomiting caused by the sea-voyage to Egypt. Other places have been fashionable from time to time for cases of tuberculosis e.g., Madeira, Devos, Canary Islands.

It is important to realize, as stressed by French physicians, that sea-voyages and sea-side places are suited to tuberculous cases. Though Laennec used to advise the sea-shore and used to put seaweed under the patient's bed in order to create an artificial marine aroma, the present day opinion is opposed to his.

(3) *Sunlight.*—The therapeutic properties of sunlight are due to the ultra-violet rays which measure from 2,100 to 3,800 Angstrom units. Normally, rays shorter than 2,900 units are filtered out by the moisture and smoke in the air. The purer the air, the greater the number of ultra-violet rays able to reach the earth's surface. Hence mountain-air is about twice as rich in ultra violet rays as the air in valleys.

Natural sunlight is definitely superior to artificial ultra-violet rays, which are often used as substitute. With natural sunlight, the effect of the ultra-violet rays is enhanced by the movement of the air and by the presence of other rays.

(4) The medicinal use of heavy metals like *gold*: This is an effective form of treatment in lung tuberculosis. Preparations of gold have been used for many years. The most used preparation is Sanocrysin, a double thiosulphate of gold and sodium, originally prepared by Moellgaard. It is given intravenously in small doses and has to be used with caution as it may damage the kidneys.

(5) Artificial pneumo-thorax or collapse of the lung. No consideration of the treatment of lung tuberculosis can be considered complete without a reference to this form of treatment. If a lung is diseased, air is artificially injected into the pleural cavity on that side in order to collapse the lung. This affords rest to the diseased part and gives it a chance to heal. The pneumothorax has to be kept up for one to three years before the condition can be considered as cured.

## Extracts.

### SURGICAL SIGNIFICANCE OF FAECAL IMPACTION.

BY ROBERT E. MULLARKEY, M.D.

(Condensed from "Northwest Medicine," April, 1941.)

The surgical significance of faecal impaction or acute constipation is one which is touched upon very lightly in the literature as early as 1913. There are no more than half a dozen short articles on the subject, and these are stories of medical curiosities rather than, as I believe, an almost daily occurrence in any large hospital.

Colon stasis or constipation may vary from delayed emptying of the stool of normal consistency to the complete obstruction of the bowel by faecal masses of stony hardness. Faecal impaction is only an extreme degree of constipation, in which faecal masses by their size, consistency and location fail to move downward in the bowel. Cathartics may cause liquid faeces and gas to pass impactions just as rocks in the bed of a river are frequently little affected by the stream. If a collection of stool produces a degree of obstruction or acute inflammation, it may become a surgical problem and a matter for decisive differential diagnosis.

Constipation is probably the most common symptom of the patients of a gastroenterologist. Severe cases almost always complain of three symptoms: (1) exhaustion, (2) nervousness, (3) gas or bloating. Occasionally a constipated patient may rather suddenly develop a condition resembling an acute surgical abdomen with or without signs of partial or complete obstruction of the bowel.

The presence of firm or hard faecal masses may be the sole cause of nausea, vomiting, pain, tenderness and abdominal distension. At the site of the impaction an area of hyperacute or suppurative colitis may develop, resulting in point tenderness, toxæmia, fever, rigidity, and leukocytosis.

Faecal impaction occurs frequently in children, producing nausea, vomiting and fever and is usually recognized promptly by the physician. Impactions may occur in adults and should always be thought of in the differential diagnosis of the acute abdomen. Faecal or barium impactions may form behind bowel tumours, strictures and obstructions, but in these situations are secondary to other pathology and are not considered here, though they may serve to call attention to the primary condition. I wish to discuss only those patients whose condition is solely due to abnormal collections of faecal matter in the normal large bowel.

#### DIAGNOSIS.

The most frequent sites of faecal impaction are rectum, descending and sigmoid colon, caecum and ascending colon, and distal transverse colon. A palpable mass may frequently be found at the

site of impaction. Light finger tip palpation should be used to localize the masses as heavy pressure tends to flatten them out.

A palpable cæcum is considered pathologic and the nature of a palpable mass in this region should always be accurately determined. A sigmoidoscopic examination will reveal presence of masses in rectum and distal sigmoid colon. A skiagram or flat plate of the abdomen, taken to show soft tissue, will localize impactions. A barium enema given under the fluoroscope may clearly demonstrate faecal masses as the contrasting medium passes by and around them.

#### TREATMENT.

Faecal impactions in the rectum, sigmoid and descending colon may be removed by repeated enemas of any type. Warm water or weak sodium chloride enemas are to be preferred as repeated injection causes little or no irritation of the bowel. Impactions of cæcum, ascending and transverse colon may be removed by repeated warm water or physiologic salt solution colonic irrigations. These should be given with the patient lying on his back. Two quarts of solution are injected slowly and with not more than three feet of water pressure. The solution is retained fifteen minutes if possible. Such an irrigation passes quickly to the cæcum and may be repeated three times a day for several days without undue irritation to the bowel.

Repeated thick barium solution enemas given under the fluoroscope and with manual manipulation of masses will frequently relieve an impaction.

Twenty-four hours preceding most surgical operations, a colonic irrigation will lessen the distressing symptoms caused by post-operative gas distension. One week after the patient has left the hospital a series of two or three colonic irrigations will often eliminate an amazing amount of undigested food and faecal matter. Postoperative anorexia is benefited by improvement of lymph circulation of the splanchnic area with beneficial reflex effects on the liver, pancreas, stomach and kidneys.

#### EARLY SIGNS OF SERIOUS GYNAECOLOGIC LESIONS

BY JAMES RAGLAN MILLER, M.D.

(Condensed from the "New York State Journal of Medicine,"  
March, 1941.)

There are certain mistakes that are commonly made early in the course of disease, errors of omission and commission which delay or make difficult the application of therapy that would otherwise be curative. I shall consider a few examples that illustrate particular points. These are chosen from cases of prolapse of the uterus, pelvic infection, and cancer which stress some of the methods of early recognition.

Many a prolapse of the uterus comes to the specialist for operation in a condition that makes him wish that he had seen the patient earlier. Some of these instances are due to the patient's own neglect, but I recall cases of prolapse with cystocele which have been carried on for years with inadequate local support, suffering repeated attacks of so-called bladder trouble. It appears that most medical men think of prolapse of the uterus in terms of backache and of mechanical inconvenience to the patient. I would suggest that you consider, more seriously than has been done in the past, the effect on the urinary system of continued distortion of the trigon of the bladder and of the ureters caused by prolapse and cystocele. Adequate repair should not be postponed until the patient presents herself as a poor risk because of age and repeated attacks of urinary infection.

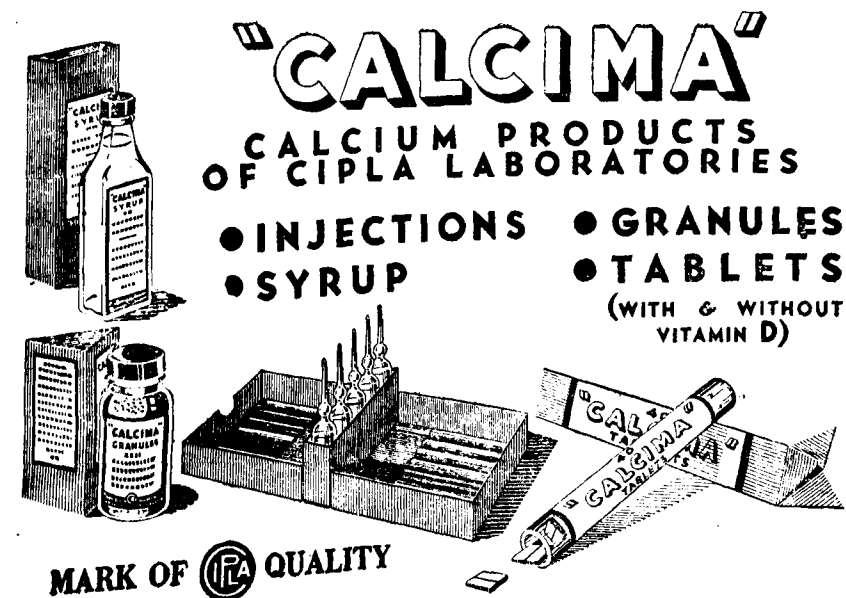
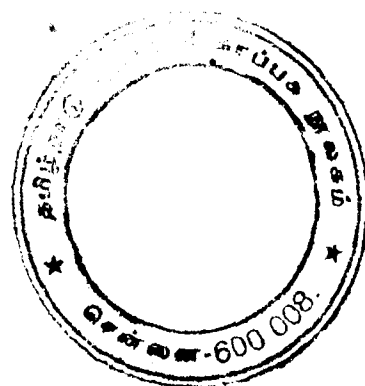
The importance of conservatism in the treatment of acute pelvic infections has been generally accepted. Few gynaecologists or general surgeons will open the abdomen if they are reasonably certain that an acute infection arises from the pelvic organs. Granted that appendicitis can be ruled out, conservative methods are the rule, particularly at the onset of infection, in the handling of which the newer sulphanilamide preparations have been found so effective. These are particularly useful in infections with the streptococcus, gonococcus, colon and Welch bacillus—organisms that produce the great majority of pelvic infections. The one particular point I wish to emphasize in the field of pelvic infections is the danger of vigorous cauterization of the cervix in the presence of acute infection. Many instances of serious and even fatal infections have been recorded, lighting up fatal infections by an over-vigorous local treatment.

The early symptoms of cancer of cervix and fundus are well known to you all and can be summarized in two words—atypical bleeding. This bleeding may occur without warning and without exertion, or it may occur following coitus or douching. All such instances of bleeding are by no means cancer, but the physician must satisfy himself as to the origin of such bleeding.

I cannot proceed further without paying my respects to the most dangerous practice of hormone treatment in the cancer age without first proving the absence of cancer. I think the hypodermic syringe filled with the latest hormones is one of the most deadly weapons that has been placed in the hands of the medical profession. This quackery, I am sorry to say, is thoughtlessly practised by members of our profession and is undoubtedly responsible for the delay in the diagnosis of many cancers of the uterus.

One of the discouraging cancers in the women is that of the ovary. We have earned, however, that many ovarian tumours, formerly called malignant, are in reality benign. These tumours cannot be distinguished clinically in the early stages when if they are malignant cure may be effected. We must rely on detecting enlargements of the ovary by repeated pelvic examinations in the cancer age. Cancer of the ovary is often slow in growing and should be more often cured. We must even be prepared to operate unnecessarily to catch the occasional early malignant tumour, for, as Schiller has pointed out, it appears likely that ovarian carcinoma does not start as a small group of malignant cells but rather occurs as a malignant transformation of neoplasm which hitherto had been benign. This concept indicates the need of prophylactic removal of ovarian growths in much the same manner that the surgeon must prophylactically remove adenomas of the thyroid.

Gynaecologists have been much interested in the Schiller iodine test and in the Kolposcope for the diagnosis of early cancer of the cervix and especially for the differentiation of cancer from other lesions. Every general practitioner should be reassured, however, by the observation commonly reported now by gynaecologists of the widest experience, that these methods have not added much to the ability to detect early cancer. It is certain that early cancers can be observed by any properly bespectacled physician, provided he will bring to bear on the lesion adequate illumination and a consciousness of cancer possibilities. The iodine solution is an excellent disinfectant to use if he wishes to take a biopsy, and it will often call his attention to the fact that the cancer has extended beyond the area that naked-eye observation would indicate. The Kolposcope is of help only to the specialist who has had wide experience in its use.



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