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The Management of Head Injuries

By ANN J. MALONEY

GENERAL CONSIDERATIONS

THERE are certain general principles of traumatic Neuro-Surgery which are virtually universal. Such statements as "Either treat adequately and early or do absolutely nothing but protect from further insult", and "The first surgery to a cerebral injury should be the definitive and final surgery",1 are constantly encountered in literature dealing with this subject. These and others like them are accepted not only because clinical experience has proven them to be the wisest policy, but also because the anatomy of the head in particular and traumatic pathological physiology in particular allow no other rational treatment. This is true both for extra- and intra-cranial penetrating wounds, since the anatomy and approach are unique.

In the first place, the head offers a more or less closely fitting, thin but tough layer of skin, muscle, and aponeurosis overlaying the cranial periosteum. There are potential spaces in the subcutaneous tissue of the scalp offering unhampered avenues for the spread of infection once it starts. There is also a rich venous communication between the subcutaneous vascular bed and the diploe of the calvarium. The brain, and more particularly, the meninges are immediately below and in fairly close approximation with the diploe. The vascular communication between the diploe and the meninges is not great but the separating bony layer is no tremendous handicap when the diploe become the seat of infection. There are numerous other equally valid reasons why even more or less superficial lacerations of the scalp must be treated with the greatest respect and diligence. Even more obvious are the reasons for the most painstaking care and the use of the very best facilities available for the surgery of intra-cranial injuries.

Since the brain and its coverings are not solidly fused to themselves or the calvarium, a very good method of decreasing trauma to such a delicate organ, there is less chance of damage from slight direct or more violent indirect impact to the head. This mechanism is not perfect, however, and it is with remarkable ease in some cases that a tear in the dura across a venous sinus or some smaller vessel, or in the
pia arachnoid, may be accomplished. Whether this be done by direct force over the laceration or after the manner of a contrecoup, it frequently occurs with little or no obvious trauma to the scalp, and occasionally with no history of sudden shifting of position, bumping, or other means. Because of these factors, the fragility of the underlying structure, the possibility of permanent intra-cranial damage, and the dangers to the patient's life must always be kept in mind when any scalp injury comes under observation. The story should always be carefully told and retold, and any questionable peripheral or central signs be given the most careful consideration. The diagnosis of intra-cranial hematoma is most frequently missed for the same reason that more general medical and surgical diagnoses are missed, namely not thinking of it.

SCALP WOUNDS AND INTRA-CRANIAL HEMATOMATA WITH OBVIOUS FRACTURE

These are discussed together because intra-cranial hematoma so frequently occurs without laceration of the scalp or with a small one.

Scalp wounds warrant the same general treatment as wounds in other parts of the body with the exception that here there is, as a rule, more contamination due to the surrounding hair, and also a much more vascular communication to the underlying bone. Osteomyelitis of any of the cranial flat bones is a most discouraging problem to treat. Because of the proximity of the hard underlying bone to the skin there is always a traumatized area of scalp around the obvious defect (excepting, possibly, incised wounds of the scalp), and the gross and microscopic hematomata in that area make fertile fields for the growth of contaminating bacteria. It becomes obvious that any manipulation that does not end in as complete cleansing and repair insofar as is possible with the best apparatus obtainable, must of necessity, be injurious. It is accepted by most that the localizing and invasion-resisting mechanisms stand a better chance of success with such conditions when left quite alone if a complete job of adequate surgical repair and cleansing may not be carried out within 48 hours of the injury.

In conjunction with attention to the story and symptoms, an equally careful palpation of every scalp laceration with a sterile examining finger should never be neglected. If any history or equivocal history of unconsciousness, dazed feeling, vertigo, nausea, or the like be uncovered, the patient should be carefully followed for the next 24 to 48 hours, and any subsequent symptom suggesting the possibility of brain lesion investigated thoroughly. In any event close contact should be kept with the patient and his actions and any abnormal tendencies (abnormal for the patient) be promptly reported. Some member of his family or intimate can do this adequately.
Since the diagnosis of extra- or sub-dural hematoma is often not evident for some time it is of utmost importance in any case coming under observation to be always suspicious and persistently inquisitive as to the subsequent course after head injury. Munro\textsuperscript{2} states that the patient is apt to have no significant symptoms at the time when a hematoma is first formed, that the injury is apt to be trivial, and that the symptoms when they develop are prone to be remissive. This is not the common type and therefore needs great diligence to detect, but the rewards are satisfactory, to say the least, to the patient who might well have gone on for months with nagging symptoms, or years with the psychotic diagnoses so frequently found in times past. Munro\textsuperscript{2} states in his paper that in a study of 310 major subdural hematomas, on a purely statistical basis, 62\% may be recognized in the “acute stage”.

The diagnosis is usually stated, in the so-called ideal case, as depending upon a history of unconsciousness followed by a period of consciousness and then a gradual lapsing back into an unconsciousness. The symptoms and history may be all the way between this unmistakable picture and one merely of chronic headaches persisting for a long period of time with the original injury forgotten or never realized. Munro says that only 10\% show the so-called typical picture.

The best of the diagnostic procedures is the spinal tap. Where there is any question of intra-cranial damage its omission is practically inexcusable. It may show little, if anything, even in the face of actual damage but this is rare. It more often shows either sound presumptive evidence or the desirability for careful observation in event of slight changes in pressure. Increased pressure, bloody fluid that fails to clear perceptibly after 15 or 20 drops, and the presence or absence of xanthochromia are all determinations that may be made at a glance, and may well spell the difference between a successfully and an unsuccessfully treated patient. Total protein and cell count are the outstanding laboratory procedures necessary on the spinal fluid in the face of a possible hematoma. Turner\textsuperscript{3} states that a lymphocytosis in the cerebrospinal fluid may be present for as long as 3 to 4 weeks after severe head injury.

Encephalogram and ventriculogram are recommended by many in the diagnosis of intra-cranial hematomas. Munro agrees that they are frequently useful, but prefers bilateral transtemporal exploration because of its combined usefulness for both diagnosis and therapy, the one procedure offering less insult than the mere diagnostic procedure of the other.

**CLOSED FRACTURES**

These are the fractures wherein the continuity of the scalp is not violated, but that of the cranium is. The subject has probably been best covered in a recent paper by the Mocks\textsuperscript{4} wherein they correlated
the results with the method of treatment in 7,031 consecutive proved or practically proved cases of skull fracture-brain injury. These were reported to them from 150 hospitals throughout the country, 487 cases being their own. They have grouped closed fractures into 4 groups as regards the symptoms and signs and their treatment. Skull fracture was either proven by X-ray or basal fracture presumptive by a short period of bleeding from one of the orifices. Palpation may occasionally reveal a depressed fracture but the majority are determined by X-ray.

**Group I**

These are classed as having a “mild concussion” as suggested by the train of symptoms and signs. These patients may show mild shock combined with a momentary loss of consciousness, or only a short period of being dazed, confused, or stuporous. In these an X-ray or bleeding from one of the orifices of the head establishes the diagnosis.

**Group II**

These patients have, with proven fracture, mild contusion or severe concussion. Associated with the mild contusion there is probably microscopic lacerations and petechial hemorrhages with localized edema or a less pronounced generalized cerebral edema. All of these give an increased pressure as shown by elevation of the cerebrospinal fluid pressure, following the Munro-Kellie doctrine. The Mocks state that in their own cases 50% were in this group alone.

The symptoms are correspondingly more marked in Group II than in Group I. These fractures are not depressed, the pathology is due to the initial blow and the subsequent cortical brain damage. One gathers that this class comprises those with a maximum of brain damage from a closed fracture without a palpably depressed area.

**Group III**

This class includes severe contusions, lacerations, and hemorrhage involving directly or indirectly the more vital centres of the brain. The pathological physiology is explained by the Munro-Kellie principle that if three constituents (blood, parenchyma, and C.S.F.) exist in a closed system, an increase in one or two causes a corresponding decrease in the remaining. Swelling of the brain following severe contusions, etc., plus increase in the cerebrospinal fluid causes constriction of the inflow of arterial blood and in the outflow of venous blood. The presence of depressed fracture or of hemorrhage may further raise the pressure. If this be allowed to persist, damage to the vital centres of the medulla may well result from either pressure or anoxia, or the brain may herniate through the foramen magnum. The diagnosis here is often more simple because of a grossly depressed area. If, however, there is wide-spread scalp contusion the diagnosis is more difficult. Whatever the case, a spinal tap will not only make the diagnosis but will be in
many instances a life saving procedure. The treatment will be discussed later.

Group IV

This group is the catch-all for the more serious types of fracture and brain injury consisting of: (a) definitely depressed skull fractures, simple and compound, (b) extra-dural hemorrhage, (c) subdural hemorrhage or collections of fluid—often persistent late signs, (d) brain abscess—a rare and late development, (e) persistent dural leaks—a rare operative indication. Their series indicated that the entities found in this group comprised 15 to 20 per cent as judged by clinical and autopsy reports. Between 5 and 10 per cent of these patients were not considered operable, placing them in the hopeless class.

The presence of a large or, as a matter of fact, a small depressed fracture, is most frequently not difficult if proper examination is carried out. Estimation of the brain damage beneath is more difficult except, of course, in the presence of grossly avulsed brain tissue. In the cases where the local area is not of much help, a thorough testing of the peripheral areas, even in the face of an uncooperative or comatose patient may occasionally produce the answer. That simple observation with the possible lesions in mind is of inestimable value, is beyond question.

OPEN FRACTURES

The diagnosis in these cases is usually evident upon inspection and if not then certainly upon palpation. Because of this it is the treatment that is the most important, and therefore little more will be said of them in this section than to mention and describe the different types.

Without Dural Penetration.—The importance of this type, other than the necessity of simple aseptic repair and debridement, is mainly the important problem of determining whether or not there is associated subdural hematoma. The dura should be inspected carefully for evidence of discoloration or tenseness, both of which, if present, are fairly obvious and diagnostic of subdural hematoma.

With Dural Penetration.—The classification used by Horrax will again be employed here in discussing these wounds. Since these are the most common type of head injury occurring in wartime, too much emphasis cannot be placed upon their importance and the necessity of correct and careful handling.

They may be divided into five more or less general types:

Gutter type.—In these cases a missile, either a bomb splinter or a bullet, plows a furrow through the scalp and bone. Whether it be a
truly tangential shot, or one in which the original path was relatively materially deflected by the skull, the outward appearance is very deceiving. Bone splinters are showered into the surrounding substance of the brain for varying areas, depending upon the relative force of the tangential blow; other debris such as hair and surrounding clothing are also spread throughout. These fragments may go even as far as one of the ventricles. Olivercrona (cited by Martin5) states that encephalitis and fungus cerebri are common complications of this type of injury, and places the mortality at 24 per cent.

Simple Penetrating Wounds—These are usually due to a more or less large single metal fragment that has carried with it fragments of bone and other debris and has lodged somewhere within the cranial confines, depending upon its impetus and direction. They frequently penetrate the ventricles, and occasionally may be found on the opposite side of the cranial cavity from their port of entrance. These, according to Olivercrona, carry an over all mortality of 37 per cent. The diagnosis in this as well as in the preceding and following types may be obvious due to the presence of a long gutter, or protrusion of a single foreign body, or multiple ports of entrance as the case may be, but generally speaking the diagnosis rests upon X-ray and the findings upon exploration, either upon the operating table or the post mortem examination.

Multiple Wounds made by Small Fragments.—Horrax15 states that these have been shown by British surgeons to be a very common type of head injury. I could find neither confirmation nor denial of this statement in a one-man review of several reliable review articles5,6 but should judge from the date of his paper—1941—that the instances might well have occurred as the result of bombing raids upon large numbers of closely, or relatively so, congregated civilians in the metropolitan and industrial centres of England. Whatever the case, the penetration of small fragments into the parenchyma of the brain sufficiently far from the gross injury is a relatively common occurrence, being for the most part bone fragments, but in many instances metal. The treatment of both is the same and will be discussed at the proper time.

Through and Through Wounds.—These are usually made by machine-gun or rifle bullets that pass from one side of the skull to the other through the brain and are mentioned as of historical interest only, for by the time they come to observation the former occupant is usually “where the woodbine twineeth”.

Wounds Involving the Air Sinuses.—This class of compound skull fracture is one of the most serious and presents not only a complex problem in postoperative management but frequently a difficult diagnostic problem. Munro7 found that 42 or 19 per cent of 218 cases of all types of compound fracture of the skull that passed through
his hands involved one or more of the paranasal sinuses. It is true that these are peacetime injuries and caused by blunt instruments for the most part (automobiles, falls, and the like), but the frequency in wartime while reduced, is still a major problem and worthy of serious consideration. Of these 42 cases only 12 or 30 per cent showed rhinorrhea, 29 had no rhinorrhea. It is seen readily that, in the light of this report from a very competent source, rhinorrhea when present is a valuable aid to diagnosis, but that its absence should make one only the more inquisitive. It is also interesting that of the 29 cases without rhinorrhea the over all mortality was 11 or 26 per cent, whereas in the cases with rhinorrhea it was two or five per cent. These last figures are percentages of total fractures with paranasal involvement and show the percentage risk as against other paranasal cases. These figures are a little unfair in that it is inferred by Munro that not all cases with rhinorrhea (which, by the way, in this paper means cerebrospinal fluid rhinorrhea) had paranasal sinus involvement by fracture. He does not make it clear where the fluid leaked from nor in how many of the cases it did not come from a paranasal sinus compound fracture. However, his total deaths for the series was 60 and of these 60, compound fractures involving the paranasal sinuses contributed 13 or 21 per cent. Sepsis, which commonly causes so much trouble in these cases, occurred in six or 14.6 per cent. Again it must be realized that we are here dealing with peacetime figures and the results of peacetime surgery. Olivercrona, in a report from Britain, again presumably based upon work done upon bombing victims, and undoubtedly under the pressure of heavy schedules, reports as high as 73 per cent mortality in these cases and states sepsis to be a frequent if not almost constant complication.

GENERAL CONSIDERATIONS OF TREATMENT PROPHYLAXIS

The principles of prophylaxis against complications in persons who will be potential candidates for generating head injuries were briefly discussed by Horrax and have been given general distribution through the daily papers and magazines. They are mentioned here only for the sake of completeness. The close-cropping of the hair, tetanus toxoid injection, and provision of each man entering a zone where possibility of injury exists with packet of one of the powdered sulfonamides are obvious advantages. If possible two packets of sulfonamide preparation should be provided, one of powder for local application upon receipt of an injury, in the case of a head injury by the first person arriving upon the scene, and the other for enteric use; the latter is to be used only if adequate treatment be delayed, and is to be taken only after a stated number of hours have elapsed since the initial dose.

GENERAL PRINCIPLES

Munro presents conclusions drawn from cultural studies upon
52 cases, and summarizes the results of Miles,\textsuperscript{9} Spooner,\textsuperscript{10} Hare and Willits,\textsuperscript{11} and Smith\textsuperscript{12} in work done in Britain. He feels definitely that, although the earliest date that is compatible with the condition of the patient is the most opportune time for the performance of operative procedure, surgery of cranial injuries may safely be put off up to 48 hours with but slight increase in the hazard of operating upon a grossly septic field.

His incidence of infection as shown by cultures was 55 per cent in the first 24 hours, with an increase of only 11 per cent to 66 at the end of the 48-hour period. He found 91 per cent positive cultures when more than 48 hours elapsed. These figures hold only if there is absolutely nothing done to the wound but protection by a sterile covering during the 48-hour period, or till the time during that period when definitive surgery is to be carried out. He further states that “if the bacteria contaminating a wound are ‘stirred with a spoon’ or the tissues contaminated by these bacteria are ‘massaged,’ a 30-minute interval between infliction of the insult and debridement is too long to wait before one deals with the infection that has been conjured up out of what was only a contamination”. He further states that with careful heed not to injure or traumatize the area sulfonamide powder may be introduced into scalp and head injuries and the so-called safe period be extended with comparative safety where the circumstances demand.

While not all agree that more than 24 hours delay may be allowed,\textsuperscript{13} most accept the work of Munro and the clinical results reported from Britain and from Germany in studies made during the present war as sufficient to warrant the delay of closure up to 48 hours if necessary.\textsuperscript{13} The main point seems to be that the fallacy that the “golden six-hour interval” must be employed in the treatment of compound fractures of the long or flat bones is a myth, and that in the face of post-traumatic complications of any magnitude such as the presence of shock, poor condition, or the desirability of transport to a centre where facilities are complete, delay in the operative procedure is not only possible, but also a distinct advantage to the successful treatment of the wound.

**Cerebral Shock**

The Mocks\textsuperscript{4} make much more of this complication to treatment than many if not most of the authors encountered. Their vehemence is convincing and the evidence that one-third of the cases collected by them that died in what they term the “better managed cases” occurred in the first six hours, lends weight to the contention. They postulate that, if rational and diligent care were exercised in the treatment of cerebral shock when present, and toward its prevention before it occurs, the higher mortality rates throughout the country, as shown by their
review of so many cases from so many different hospitals, would be reduced 25 to 50 per cent.

It must be watched for in the mildest cases of head injury and expected in all of the more severe ones. It is described as the picture of direct or indirect trauma to the vital cerebral centres grafted on to the condition of ordinary traumatic shock. Disturbed consciousness ranging from a dazed condition to deep coma usually accompanies it. Slow shallow respirations, a slow pulse, and low diastolic pressure are said to be present in addition to the ordinary signs of shock. This is confusing since all of the above except slowed pulse and respirations are part of the picture of secondary shock. Possibly the slowing of respirations and cardiac rate may be due to local action in the brain of trauma, or to the effect of anoxia upon the respiratory and cardio-accelerator centres, when increased intra-cranial pressure is present in sufficient degree.

That this complication be circumvented whenever possible the Mocks have set worth a few principles for the conduct of every patient with head injury:

1. Transfer the patient to a bed, wrap in blankets, and apply heat. Patient should not be moved off the bed or overly disturbed till good condition is evident. If shock supervenes no procedures at all may be performed other than those for treating the shock.

2. No operative procedures excepting those absolutely necessary. Suturing, reduction of fractures that are associated with the head injury, or immediate operations are added insults that can be delayed with but few exceptions.

3. Only slight sedation, morphine rarely and then never over 1/6 grain.

4. Transfusion, plasma, or fluids where necessary.

5. Oxygen may prove very valuable.

Observation of the course of the patient is held to be the most valuable criterion for determining when the danger period is over. This includes blood pressure, temperature, and respirations, along with his appearance and demeanour.

Sedation seems to be the centre of a great deal of controversy. All agree that only small amounts should be given, and many believe that none are required. Extreme restlessness, delirium and severe headache are the most outstanding complaints for which sedation is ordered. The etiology of these signs and symptoms is swelling and compression of the component elements inside the skull, and prompt relief of the increased pressure will relieve the situation. The Mocks
feel that delay in the use of hypertonic solutions and lumbar puncture accounts for the ineffectiveness often complained of.

DEHYDRATION

This may be accomplished with any one of a number of hypertonic solutions injected intravenously. Some of the more common and one uncommon are presented:

Dextrose and Sucrose.—50 cc. of a 4 to 60 per cent solution.

Magnesium sulfate.—A solution with a concentration of 15 per cent is recommended as both reducing the arterial blood pressure, the intra-cranial edema, and having a generally sedative effect upon the patient, by Ghetti. 14

Concentrated Serum.—Used by Turner 3 in Britain. There are many that disagree with its usage, pointing out the possibility of making the patient worse by reaction.

Colloid Supplement.—Jorns 17 used a combined solution of 7 per cent sodium chloride with 3.5 per cent polyvinyl alcohol. He evolved this because he felt that the usual hypertonic solutions produced insufficient and evanescent effect. Experimental and clinical evidence has proven the usefulness of this mixture. He gave 50 to 100 cc. and repeated if necessary.

Diet.—Like the giving of intravenous fluids by vein in dehydration, oral control of hydration as well as dehydration is too often overlooked. It is not rapid but in those cases where there is adequate time, the dietary method is by far the most effective.

There is much controversy about the usefulness and dangers of dehydration therapy for cerebral edema and increased intra-cranial pressure. The chief complaint is that a dangerous dehydration of the whole patient is accomplished and that the means complicates the end. It seems to be well accepted by at least a few reliable writers 16, 4 that intelligent and careful dehydration in these cases is often the most effective and sensible treatment.

LUMBAR PUNCTURES

The performance of lumbar puncture in patients with either questionable or presumptive intracerebral injury is without question the most important single preliminary procedure, and its neglect is inexcusable. Its judicious use is of the utmost importance. It not only may tell of an increase in the intra-cranial contents, but the presence or absence of cellular elements and their type often solve a differential diagnosis. There is no more prompt way of reducing increased intra-cranial pressure, and that in itself at times may be a life or function saving procedure. Used with proper dehydration
therapy it is an indispensable adjunct to the careful treatment and following of intra-cranial injury and repair.

**Preparation for Cerebral Surgery**

This, and the following subjects, are more or less, with the general principles excepted, out of the scope of a student's paper, and will be discussed only briefly.

No preparation should be carried out until the definitive and final surgery is at hand. This applies to scalp wounds as well as cranial and intra-cranial procedures.

First, stereoscopic X-ray films should be made, in lateral as well as A-P and P-A.

The whole head should be shaved carefully, and the shaven scalp carefully examined.

A brief neurological examination should be carried out to ascertain the final status before operation.

If all neurologic data are noted and the patient not drowsy or unconscious, a small dose of morphine may be given one-half hour before operation.

Anaestheisia must be carefully and competently given, and if so the agent is at the discretion of the anaesthetist.

**Scalp Wounds**

These should be treated in general with a few anatomical modifications in the same manner as intra-cranial wounds. The chief difference is that with an intact calvarium copious irrigation is the rule (five to seven litres of sterile physiological saline) whereas in repairing intra-cranial wounds the more or less accepted method now is to do no irrigation, but to use suction alone. Munro is one of the most avid endorsers of the last rule.

The procedure briefly is one of thorough washing of the area surrounding the wound while the wound is covered with a sterile pad. This accomplished, the wound is uncovered and with bleeding controlled, debridement of all dead and contused tissue commenced, under novocaine infiltration in scalp cases. Copious irrigation with complete debridement is carried out. If there be tears in the periosteum they are best sutured after palpation has determined the absence of fracture, or even in the presence of a small linear fracture that occurred in a patient with no symptoms or signs of intra-cranial complications. Galea should be sutured to galea if such a tear occurs, and the remaining layers included in a layer of interrupted sutures. It is best to precede all suturing with a sprinkling of sulphonamide powder, but this is elective in so-called clean cases. A light dry sterile dressing is applied and bed rest ordered for 24 hours for observation before discharge.
Subdural Hematomas

These are usually of doubtful location and the operation is correspondingly exploratory; the necessity of entrance on the opposite side should exposure of the dura on the first side prove fruitless, must be kept in mind. Incisions are selective, some preferring triradiate, some straight line, and some semicircular. Burr holes are first made exposing the dura for inspection. Two are commonly made in the transtemporal approach, about two inches apart. Should the dura appear normal through the burr hole the periosteum and muscle layers are closed separately, with the skin, and the other side is explored. Upon finding a clot extradurally it is evacuated, as much as frees easily, and bleeding points sought for. If a bleeder is found, and it may be presumed to have been the cause for the hematoma, it is tied off, the dura carefully inspected for signs of underlying collection of fluid, and finding none, the retreat begun. If more bleeding is suspected due to inability to find the source of the hemorrhage, a drain is commonly left in the wound for 36 to 48 hours to allow for drainage should the bleeding recur. If not, the muscle layers are sutured together over the cranial defect and the superficial layers sutured.

The procedure for subdural hematoma is the same except that the dura is incised and clot evacuated. If the bleeding source is found and ligated, the dura may be tightly sutured and the same manner of retreat carried out.

Closed Fractures

The approach is determined in these cases by X-ray evidence and the incision is made directly over the defect. The bone fragments should be removed and the underlying dura inspected as previously described, and dealt with according to the findings.

Open Fractures

A. Without Dural Penetration

These are treated simply by an aseptic repair and debridement with the added precaution of inspecting the dura for subdural injury.

B. With Dural Penetration

While the different types vary in manner of occurrence, the principles of repair are essentially the same in all. There must be:

1. Adequate exposure—this usually involves enlarging the portal of entrance with rongeurs and smoothing the skull edges.

2. Control of bleeding—bleeding from the diploe is best controlled by bone wax. Electro-coagulation equipment is invaluable in controlling bleeding, except in the speech area.

3. Debridement—This is a tedious and painstaking job. It is done with not too strong suction. All of the macerated brain
tissue, clots and foreign material are sucked out, being careful not to injure uninvolved tissue. Having the patient, if he be under local, cough or otherwise strain may be helpful in extruding clots and macerated tissue. A soft rubber catheter should be used with great delicacy.

Foreign bodies, if freshly imbedded, and easily accessible, should be removed, but under no circumstances should the operator prowl about normal tissue for remote pieces. They, in all probability, will never cause complications, and if they do, less damage will be wrought by a direct approach to them at that time.

Metal particles may be removed, if they are close to the defect, by an electro-magnet, or if obvious to the operator’s eye may be carefully lifted out by fine forceps.

Useful adjuncts to the described methods of hemostasis are the use of silver clips or muscle grafts.

4. Closure—The dura is closed over the cortical scar, making a relaxing incision laterally if necessary. Periosteum may be used as a dural graft if necessary. No attempt is made to replace the bony defect.

The scalp is closed by two layers of interrupted silk sutures, one in the galea and the other in the skin. Compound fractures involving the paranasal sinuses are treated essentially the same but must be packed open.

**BIBLIOGRAPHY**

Penicillin

By RAMSAY W. GUNTEN

A. Experimental

DISCOVERY: Pasteur and Joubert in 1877 first described the phenomenon of microbial antagonism. They observed that certain micro-organisms inhibited the growth of the anthrax bacillus and suggested at the time that this might have a therapeutic application. Since then other examples of bacterial antagonism have been reported. The inhibition of growth is believed to be due to metabolic products formed by the antagonistic organism. These products are now termed “antibiotics”. Pyocyanase, actinomycetin and tyrothricin are antibiotics which have been investigated for possible therapeutic properties in human diseases.

The antibiotic penicillin was discovered in 1929 by Fleming when he observed that a contaminating mould, Penicillium notatum, caused lysis of staphylococcus aureus colonies growing on an agar plate. Keen interest in problems of antisepsis prompted him to study this mould further. He cultured it in broth and found that the filtered culture medium was lethal to staphylococci in a dilution of 1 in 800. Further experiments revealed that “penicillin”—the name which he applied to this potent antibiotic—was also extremely effective against other pyogenic cocci and the diphtheria bacillus but not against the colon-typhoid group or the Haemophilus influenzae. Attempts at extraction and purification proved penicillin to be extremely labile and easily destroyed by acids, alkalies and high temperature. Fleming tried injecting it intravenously and intraperitoneally into rabbits and mice, and found that it was not toxic. He published a report of this highly bactericidal, non-toxic substance and suggested its use as an antiseptic in wounds but its extreme lability discouraged further attempts at purification. Fleming used pencillin for the differential culture of the influenza bacillus and certain susceptible cocci found in the throat.

Early therapeutic investigations. In 1939 Chain and Florey at Oxford decided to investigate the antibiotics in a systematic manner. Fortunately, one of the first they chose was Fleming’s penicillin. Having corroborated his observations that penicillin was lethal to many pyogenic cocci and non-toxic to animals, they set about extracting and purifying it and were able to obtain a crude penicillin in sufficient amounts for a few experiments. The therapeutic trials were carried out on mice infected intraperitoneally with strep. pyogenes, and staph. aureus, and in the thigh with Clostridium welchii. Penicillin was injected sub-cutaneously at frequent intervals for 10 days. The results were astounding. In each case the 25 controls died but 24 out of 25 of the treated mice survived.
Large scale investigations were immediately begun at Oxford to learn more about this amazing substance which could cure such fatal infections in laboratory animals. Methods of production and purification were improved and, for convenience, a unit of strength of penicillin preparations was devised. Glass cylinders with open ends were placed upright on agar plate seeded uniformly with staphylococcal colonies. The unknown preparation was placed in the cylinder and allowed to diffuse into the surrounding agar, preventing growth of staphylococcal colonies for a variable distance from the edge of the cylinder. One Florey or Oxford unit is the amount of penicillin which, when dissolved in 1 cc. of buffered solution, will produce a zone of inhibition 24 mm. in width. This unit is purely arbitrary but its use facilitates correlation of experimental results. Other standardization procedures have been devised.

Abraham, Chain and Florey\(^5\) reported in 1941 the first trials with penicillin on human subjects. They used the sodium salt of penicillin containing 40 to 50 Florey units per mg. It was given intravenously by continuous drip to patients with hopeless staphylococcal and streptococcal infections. Some cases survived, all improved, and failures were due not to toxicity of the drug but to insufficient amounts, for the yield was still very small.

Purification and chemical structure. The greatest obstacle to progress in penicillin therapy has been the difficulty in obtaining sufficient supplies of relatively pure material. The drug is so unstable in the crude form that tedious extraction methods must be used and these have been perfected only by the most intensive efforts of chemists in the U.S.A. and England. Spores of the mould Penicillium notatum are inoculated on culture medium of a certain definite composition. When the mould has grown to form a greenish felt-like moss on the surface, the liquid medium is withdrawn. By the method of Abraham and Chain\(^9,11\) the medium is extracted with amyl acetate at pH 2 then into water at pH 6 with addition of barium hydroxide. Absorption of impurities by charcoal, chromatographic separation, reduction with an aluminium-mercury couple and further extractions produce a white barium salt of penicillin containing 500 units per mg. This is a much more concentrated material than that used in the first human trials (40 to 50 units per mg.), yet Florey and Jennings\(^12\) have shown that it is less toxic. The sodium salt of penicillin is light yellow in colour and may be kept for some time in aqueous solution. Penicillin in its acid form, is hygroscopic and quickly inactivated in air so that it is used clinically in the form of its more stable sodium and calcium salts.

Penicillin is an acid, containing carbon, hydrogen and nitrogen. Its bactericidal power increases with the percentage composition of
nitrogen. It has an estimated molecular weight of 640 and the proposed empiric formula for the barium salt is C24 H32 O10 N2 Ba.10,11

Two break-down products, penicillic acid and penicillamine have been isolated and studied.33 Since publication of further details on structure and synthesis of penicillin has been prohibited, these observations made in 1942 are the only ones available. One can reasonably assume, however, that because the molecule is of relatively low molecular weight and is not a complex protein like so many other biological preparations, synthesis may be accomplished in the near future.

Bacteriology and Pharmacology. Various bacteriological tests5 have proved penicillin to be effective against the following organisms: gonococcus, meningococcus, pneumococcus, staphylococcus aureus, streptococcus pyogenes, strep. hemolyticus, clostridium welchii, cl. oedematiens, cl. septique, cl. tetani, b. anthracis, actinomyces bovis and streptococcus viridans. It is relatively ineffective against: mycobacterium tuberculosis, b. coli, the typhoid, paratyphoid and dysentery bacilli, Brucella abortus and melitensis, Friedlander’s bacillus, vibrio cholerae, past. pestis. It should be noted that different strains of pneumococcus, strep. viridans and anaerobic streptococcus, vary in their susceptibility.

The exact mechanism of action of penicillin is unknown but like the sulphonamides it is bacteriostatic rather than bactericidal.5,14 It prevents multiplication of the susceptible organism. Gardner has reported that giant forms are produced when bacteria are treated with penicillin. In combatting disease, penicillin prevents increase in the number of infecting organisms and allows the natural defenders—leucocytes and serum antibodies to finish the job. Unlike the sulphonamides, penicillin is not toxic to leucocytes so the danger of agranulocytosis, always present in cases of intensive prolonged sulphonamide therapy, will not be encountered.

Abraham, Chain and Florey5 also pointed out that penicillin did not harm cells grown in tissue culture or produce any inflammation on the delicate tissue of a rabbit’s brain. Even more important was their observation that penicillin retains its potency in the presence of pus and tissue autolysates. In this respect also, penicillin differs from the sulphonamides and the fact is of great significance in the local therapy of infected wounds and abscesses where such products of suppuration are abundant.

Organisms do develop resistance to penicillin if repeatedly cultured in its presence. Rammelkomp and Maxon16 report a 16-fold increase in resistance in a strain of staph. aureus cultured before and after penicillin therapy in a human infection. But Keefer24 has encouragingly pointed out that this increase in resistance is accompanied by a corresponding decrease in virulence. Pencillin is very effective against
organisms already resistant to sulphonamides, particularly in gonococcal and pneumococcal infections.8,24

According to the studies of Rammelkomp and Keefer,22 when a 20,000 unit dose of penicillin is injected intravenously there is an immediate rise in its serum concentration, followed by an abrupt fall so that at the end of three to four hours, none is detectable. It appears almost immediately in the urine in large amounts and continues to be excreted as long as there is any in the serum. Some believe that penicillin may have a diuretic effect. The maintenance of an adequate blood concentration is therefore rather difficult and Florey has aptly likened it to “trying to keep a bathtub full of water when the plug is out”. With intramuscular injection there is not the initial high concentration but a moderate level is maintained for two to three hours. It has been estimated that a concentration of 0.15 units per cc. of serum is necessary for adequate therapy.

When penicillin is injected into joint cavities, the pleural cavity22 or the sub-arachnoid space,19 minimal amounts appear in the urine and blood, and a high concentration is retained in the injected cavity after 24 hours. This would indicate that in the treatment of acute suppurative arthritis, empyema, and meningitis, local therapy is indicated. Intravenous penicillin does not appear in the cerebro-spinal fluid in significant amounts.22

Given orally, penicillin is destroyed by the acid of the gastric juice.21 It is ineffective rectally because it is destroyed by “penicillinase”, an enzyme produced by b. coli. Other airborne organisms are capable of producing this enzyme.32

B. CLINICAL

General Discussion: Following the initial clinical successes with penicillin in England, large scale investigations on methods of production and therapeutic application were carried out in that country and in the United States. The original enthusiasm has not been unwarranted, for, although penicillin is not a panacea for all ills, its discovery marks a significant advance in the fight against disease. Because of the limited quantity of the drug available, most of the trials have been on conditions refractory to sulphonamide therapy or those likely to occur in war surgery. The mortality in staphylococcal septicemia has been reduced from 90 per cent to 30 per cent. Osteomyelitis, mastoiditis, hand infections, pneumonia, empyema, meningitis, eye infections, skin infections, gonorrhea, burns, war wounds and compound fractures are but a few of the many conditions in which penicillin therapy is more efficacious than anything used heretofore.

The technique of pencillin therapy is not easy. The services of a bacteriologist, surgeon and internist must be called upon to treat many
cases. The bacteriologist must first find out if the organism producing the condition is susceptible to penicillin and he then must follow the case by taking periodic blood or wound cultures to be sure the dosage is adequate. In cases of generalized sepsis, treatment is continued for weeks or months at a time, and one does not see the dramatic drop in temperature with penicillin therapy that one is accustomed to note in sulphonamide therapy. Such signs as increase in appetite, gain in weight, clearer mentality, drop in white count to normal, rise in red count, are more valuable criteria of improvement than is the temperature chart. Parenteral administration of a drug for two to three weeks is hard on patients, and penicillin must be given at frequent intervals in order to maintain an effective blood concentration. An intramuscular injection administered inexorably every three hours, day and night for a month, would be enough to unnerve even the most stoical individuals. Or if intravenous administration is used, there is the problem of thrombosis to encounter. But the results from penicillin therapy have amply justified its use, despite these difficulties, for doctor and patient.

High antiseptic power, non-toxicity to tissues and leucocytes, retention of potency in the presence of pus and tissue autolysates makes penicillin ideal for local therapy. It may be administered in the form of a solution, wax, or powder. In infected wounds and abscesses, the surgical principles of wide incision and drainage must be modified if penicillin is to be used, for the drug has to be in contact with the infected surface for a long period and too free drainage would allow the vehicle to run out. Often such wounds are sutured, leaving in a fine rubber tube through which pus is aspirated and penicillin reinjected. This technique has been used in the Florey method of treating acute mastoiditis, in boils, carbuncles, empyema, etc. It should be stressed, however, that any loculated masses of pus should first be broken down if penicillin is to have access to all infected parts. This applies to cases of empyema particularly. In eye infections, superficial skin infections and burns, penicillin is applied directly as an ointment or powder. In meningitis, the solution is injected intrathecally.

Preparations, routes of administration and dosage. For systemic therapy, penicillin is supplied as its yellow sodium salt in ampoules containing 5,000, 10,000, 25,000, 100,000, and 1,000,000 units. These should be stored in a refrigerator until used. The contents of the ampoule may be dissolved in distilled water, isotonic saline, or 5 per cent glucose in saline. For intravenous injection, if this is to be done by syringe, a solution containing 1,000 units per cc. of saline is made up, and is usually injected every three hours into the vein in doses of 10,000 to 15,000 units. Some clinicians prefer to dissolve the dose of penicillin in 5 per cent glucose in saline and to administer it by continuous intravenous drip.
For intramuscular injection, the same dose is given every three hours, into the gluteal region, in saline containing 5,000 units per cc. No sloughing results from the intramuscular injection. Slight pain may persist for several hours.

As a rule, an adult receives 100,000 units daily in cases of generalized infection, but this is reduced or increased depending upon clinical signs, blood culture reports, and blood counts.

For local therapy the calcium salt of penicillin is used:

(a) As a solution containing 250 units per cc. in water.
(b) In sulphanilamide powder containing 2,000 to 5,000 units per gram.
(c) As an ointment in a wax base containing 600 to 800 units per gram.

DISCUSSION OF INDIVIDUAL CONDITIONS:

*Staphylococcal septicæmia.* Because of its refractoriness to sulphonamide therapy, this condition more than any other has been treated with penicillin. Many cases which failed to respond to any other treatment, including autogenous anti-serum, have been completely cured. Doses of 80,000 to 160,000 units daily are administered for one to three weeks. The blood culture soon becomes negative, appetite improves, the white cell count falls to, or rises to, normal. Blood transfusion is a valuable adjunct to penicillin therapy. In cases complicated by acute ulcerative endocarditis the results are not as good.\(^4\),\(^5\),\(^24\)

**OSTEOMYELITIS — Acute.** Acute haemotogenous osteomyelitis responds rapidly to penicillin. Doses of 10,000 units intravenously or intramuscularly may be given to a child. Incision over the involved bones may or may not be employed. In a few days there is decreased pain and temperature of the affected part, and X-ray reveals a rarefaction in the involved bone. This observation was at first disturbing but when it was discovered that recalcification occurred in two or three weeks after clinical recovery, it was assumed that the rarefaction indicated the absorption of necrotic products. There may be a rise of temperature coincident with the period of rarefaction but this should be disregarded.\(^20\),\(^21\),\(^24\)

**Chronic.** Chronic osteomyelitis with sinus formation does not respond as successfully to penicillin therapy. General and local treatments are combined. In the case of the latter, a catheter is inserted into the draining sinus and penicillin solution is injected two or three times a day. The sinuses soon become sterile for pyogenic cocci but recurrences are frequent. It is clear that further investigation is necessary before this condition may be listed under those which penicillin has conquered.\(^24\),\(^31\)
Cellulitis. Streptococcal and staphylococcal cellulitis of the face and oral cavity is effectively treated by penicillin. Moribund cases with cavernous sinus thrombosis and bacteræmia have responded dramatically to systemic treatment. In cases where incision had been performed, the wounds became sterile in a few days.5,18,21

Pneumonia. Few cases of pneumonia have been reported because this condition is so well controllable by the sulphonamides. Penicillin is very effective against the pneumococcus and cases have been cured by the administration of 100,000 units in three days.

Empyema. Streptococcal, pneumococcic and staphylococcic empyema will respond to penicillin. Injection of 30,000 units in saline directly into the cavity once or twice a day is the recommended treatment. Thoracotomy may be necessary. It must be emphasized, however, that this is not irrigation of the empyema cavity. Penicillin must be in contact with the infected area for six to eight hours and the solution should, therefore, be left in the wound. Periodic aspiration of pus is necessary.21,24

Meningitis. Because penicillin does not appear in the cerebrospinal fluid after parenteral administration, intra-thecal injection is necessary in the treatment of meningitis. The dose is 10,000 units in saline once or twice a day. Ordinary dosage by the systemic route is given at the same time. There have been cures of staphylococcal and pneumococcal meningitis reported and the failures have been due to not administering penicillin intra-thecally. These types of meningitis were refractory to sulphonamide therapy and universally fatal. When pneumococcal meningitis is accompanied by endocarditis, penicillin is ineffective.19,22,24

Gonorrhea. Penicillin has been effective in sulphonamide-resistant gonorrhea. Sixteen doses of 10,000 units each given every three hours render the patient asymptomatic and bacteriologically negative in 9 to 48 hours. This is most encouraging in view of the fact that gonorrhea causes so much lost time among army personnel. The British army used penicillin against gonorrhea in North Africa and one observer described its effect on the urethral discharge as “like turning off a tap”.23,24

Syphilis. Mahoney28 has reported four cases of seropositive primary syphilis treated by 25,000 unit parenteral doses every four hours for eight days. The lesions were sterile in two days and the serum later became negative. However, the final answer as to the efficacy of penicillin in the treatment of syphilis cannot be given until more trials have been made and the treated cases followed for a period of years. Herrel29 has reported a case of tertiary cutaneous syphilis which cleared up, yet the serum remained positive.
Actinomycosis. Although the actinomyces bovis is susceptible to penicillin by bacteriological tests, any cases of actinomycosis treated with the drug have failed to respond.24

Sub-acute Bacterial Endocarditis. The streptococcus viridans is destroyed by penicillin in vitro. High hopes were held that cases of sub-acute bacterial endocarditis could be cured with penicillin but the results have been discouraging. Intensive penicillin therapy over periods of one to two months has been unsuccessful in curing the disease. While penicillin is being administered, the patient feels better, the white and red blood counts become normal, and the blood is negative to culture, but as soon as the treatment is discontinued there is immediate relapse. It would appear that penicillin cannot abolish the activity of the lesion on the heart valve.24

Skin and Eye Infections. Cases of blepharitis, acute conjunctivitis, sycosis barbae, impetigo and eczema have been successfully treated by the local application of penicillin powder or in ointment form.

War Wounds. The experience of British army surgeons in North Africa and Sicily has proved that in long-standing wound sepsis local treatment with penicillin is ineffective. But when the wounds are treated earlier in combination with systemic penicillin therapy the results are much better. The wounds treated were of two types:

(a) Recent large, soft, tissue wounds. These were treated by suture, leaving in two small rubber tubes through which penicillin could be injected or pus aspirated.

(b) Compound fractures. This type of injury is particularly susceptible to infection with the subsequent development of osteomyelitis. The principle of treatment was conversion of compound to simple fracture by suture after penicillin powder had been applied and debridement carried out, followed by parenteral administration of 100,000 units of penicillin a day for a week. It was estimated that the use of penicillin in major wounds saved five to six weeks in hospital—a considerable achievement.25,26

Gas gangrene. Cases of wounds infected with clostridium welchii were given anti-toxin and parenteral penicillin for two to five days. If treated early, the results were remarkably good. Penicillin used alone would prevent gas gangrene in wounds but would not check the infection once started.17,25

Burns. Application of penicillin powder will prevent infection of the burned surface by streptococci and staphylococci and will, therefore, greatly aid the "take" of subsequent skin grafts. The development of "gram-negative pus" from pseudomonas pyocyanea and b. proteus will
occur in the presence of penicillin, but does not seem to affect the skin grafts. These results by British investigators are not corroborated by reports from the United States, where gram-negative pus has been thought to prohibit good skin grafting.

**SUMMARY**

Penicillin is a highly effective therapeutic agent in the treatment of human infections. Just as prontosil in 1935 heralded the arrival of a variety of potent sulphonamide compounds, so the eventual synthesis of penicillin will bring in its wake many new drugs with even greater chemotherapeutic effects. Medicine is well on the way toward conquest of the diseases caused by micro-organisms. Great will be the day when comparable advances have been made in the realm of the neoplastic diseases.

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SUMMER DIARRHEA IN BABIES

Casec (calcium caseinate), which is almost wholly a combination of protein and calcium, offers a quickly effective method of treating all types of diarrhea, both in bottle-fed and breast-fed infants. For the former, the carbohydrate is temporarily omitted from the 24-hour formula and replaced with 8 level tablespoonfuls of Casec. Within a day or two the diarrhea will usually be arrested, and carbohydrate in the form of Dextri-Maltose may safely be added to the formula and the Casec gradually eliminated. Three to six teaspoonfuls of a thin paste of Casec and water, given before each nursing, is well indicated for loose stools in breast-fed babies.

Please send for samples to Mead Johnson & Company, Evansville, Indiana.
Primary Atypical Pneumonia of Unknown Aetiology

By K. Eric Rogers, M.D.

During the past decade much attention has been directed to a type of pneumonia which differs in many details from the familiar pneumococcal lobar pneumonia.

The first clinical description of the condition, which is at present termed primary atypical pneumonia of unknown aetiology, was given by Bartels in 1861. Because Bowen called attention to a form of "pneumonitis" in 1935, he is credited with the arousing of recent renewed interest and investigation of this increasingly important subject. It has been referred to by many names such as "virus pneumonia", "acute interstitial pneumonitis", and "atypical bronchopneumonia".

Carefully investigated series of cases have been reported recently in the United States and in England. Some of these are tabulated in Table I. Many reports include plates illustrating radiological and pathological findings.

### Table I

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<th>No. of Cases</th>
<th>Average Days Febrile</th>
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Clinical Findings

The onset of the illness is usually gradual. Investigators\textsuperscript{15,16} agree that the incubation period is between seven and 21 days. When the patient is first seen, a history of frontal headache (often mistaken for sinusitis\textsuperscript{14}), malaise, generalized aching pains with chilly sensations during the past few days, is given. Generally, there is a persistent cough with a small amount of tenacious mucoid sputum. Pleuritic pain is rare,\textsuperscript{3,10,14,15} although retrosternal soreness suggesting tracheitis is fairly common. Drew\textsuperscript{3} states that rusty or prune juice sputum has never been reported in primary atypical pneumonia and its occurrence should suggest that the diagnosis be reviewed. In Drew's series there were three cases of frank haemoptysis.

On inspection, the patient does not present the appearance of a seriously ill pneumonia case. Herpes is very rare. In the great majority of cases, in spite of a markedly elevated temperature, the pulse rate and the respirations are within normal limits. This is a reassuring sign in the few patients who appear to be seriously ill.

Initial physical examination reveals slight pharyngeal injection. In the early stage, abnormal chest findings are conspicuous by their absence. Some observers\textsuperscript{3,8,13,15} state that fine moist râles and areas of dullness appear as the illness progresses. The abdomen is flaccid. Lymphadenopathy is absent.

The patient's course is variable. The temperature may return to normal in the first 24 to 48 hours, or it may rise as high as 104\textdegree, then fluctuate between 101\textdegree and 103\textdegree, and subside by lysis in seven to 10 days. The pulse remains normal throughout. Râles appear about the fifth day and gradually clear in seven to 14 days.

Sputum investigation for pneumococci is negative.\textsuperscript{13} A transient albuminuria is present in some cases. The E.S.R. may be elevated. Some authors\textsuperscript{7,13,15} report a leucopenia in the early stages. There is a tendency to leucocytosis as the disease progresses.

The complications reported have been encephalitis,\textsuperscript{14} rashes, meningismus, jaundice, small pleural effusions\textsuperscript{14} and otitis media.\textsuperscript{3,18} The latter is the most common.

Incidence

Primary atypical pneumonia may occur during any season, but as Table II indicates, the great majority of cases occur between October and March.

Diagnosis

The above signs and symptoms make one suspicious of the diagnosis, which is confirmed only by radiography of the chest. This is performed in most cases because of persistent cough or pyrexia. The film invari-
TABLE II

Seasonal incidence of 312 cases in the series of Drew, Rhoads, Murray and Gallagher.

ably shows the amount of lung involvement to be much greater than was suspected from the clinical findings.

Radiographic Findings

The increased frequency of the confirmed diagnosis of primary atypical pneumonia of unknown aetiology is due to the more frequent use of chest radiograms. Investigators\textsuperscript{2,3,8,10,15,16,17} agree that there is no typical radiological appearance. Radiographic evidence of chest
involvement appears about the fourth day of illness. These findings precede detectable abnormal physical findings by at least 48 hours. Drew\(^3\) describes two main types of lesions.

**Type I (commoner)**

A woolly area of consolidation varying from a patch the size of a quarter to partial or complete involvement of a lobe. This area is less dense and more mottled than in pneumococcal pneumonia.

**Type II**

This lesion radiated from, and was more conspicuous near the hilar region.

McCarthy\(^6\) states that in basal lesions of any type the diaphragm remains uninvolved. The lower lobes are most frequently involved.\(^3,8,13\) Pleural adhesions rarely develop. Pleural fluid is a rarity.

There is no relation between the severity of the cough, the duration of the fever and the extent of the pulmonary lesion revealed by the radiogram.

**Pathological Findings**

_Gross_—The bronchial mucosa is congested and may be covered with a mucoid or mucopurulent exudate. Adams\(^11\) reports proliferation and sloughing of bronchial epithelium. On section, the lung surfaces are red, mottled with gray. Small consolidated areas can be detected. Hilar lymphadenopathy is usually present.

_Microscopic_—The lesions are interstitial in nature.\(^5\) “The capillaries are hyperaemic and the interstitial tissue is crowded with lymphocytes and mononuclears, with only very few polymorphonuclear leucocytes” (Saphir's second case). Alveolar walls are intact. Monocytic peribronchial infiltration is present. Adams\(^12\) describes cytoplasmic inclusion bodies in the diseased epithelial lung structures. Saphir's first case showed inclusion bodies of a different type. There are very few bacteria in the lung, none predominating.

**Aetiology**

To date no single cause for primary atypical pneumonia has been discovered. Several writers\(^3,18\) mention the similarity of the clinical, physical and radiographic findings in primary atypical pneumonia, psittacosis and Q fever. The latter two conditions are caused by viruses. Attempts to establish a relationship between the influenza virus and primary atypical pneumonia have failed.

**Differential Diagnosis**

(1) **Influenza:**

Primary atypical pneumonia may be differentiated with certainty from similar conditions classed as influenza, by means of the X-ray. In
primary atypical pneumonia, the lesion is more localized than in acute tracheobronchitis or influenza.

(2) Early pulmonary tuberculosis:
The woolly mottling lesion, particularly in the upper lobe, is difficult to differentiate from pulmonary tuberculosis. The greater enlargement of hilar lymph glands in primary atypical pneumonia is a useful distinguishing feature. The striations extending from the consolidated area to the hilar shadow are less marked in primary atypical pneumonia according to Drew. Rapid resolution favours the diagnosis of primary atypical pneumonia.

(3) Pneumococcal Pneumonia:
This condition is distinguished by its dramatic onset, pleuritic pain, herpes labialis, leucocytosis and the finding of pneumococci in the sputum.

(4) Bronchiectasis:
Bronchography will differentiate conclusively the rare case of bronchiectasis which cannot be diagnosed clinically.

Treatment
There is no specific treatment. A patient with primary atypical pneumonia should be confined to bed until the temperature remains normal. He should receive liberal fluids and a normal diet with added sodium chloride when there is marked perspiration. Investigators\textsuperscript{3}•\textsuperscript{4}•\textsuperscript{7}•\textsuperscript{13} emphasize the finding that sulphonamide drugs have no effect on this condition. Codeine is useful in controlling the annoying cough. Salicylates help relieve the aching and malaise, which are prominent during the early part of the disease. In severe cases with respiratory distress oxygen therapy is indicated. Chest films should show complete resolution before the patient returns to full activity.

Prognosis
The condition is rarely fatal except in cases associated with some other condition such as chronic heart disease. Adams\textsuperscript{12} reports a high mortality rate (83\%) in premature infants. The mortality rate among full-term infants was eight per cent. Although the mortality rate for the 651 cases listed in Table I was 3.5 per cent, it is generally agreed that primary atypical pneumonia is an essentially benign syndrome with a mortality rate of less than one per cent.

**Summary**

1. Primary atypical pneumonia of unknown aetiology differs in many details from pneumococcal pneumonia.

2. Primary atypical pneumonia pursues a varied clinical course. The prognosis is good if the condition is unaccompanied by serious complications, for example, myocardial degeneration.
3. A diagnosis can be made with certainty only with the aid of X-ray films of the chest.

4. There is no relation between the severity of the cough, the duration of the fever and the extent of pulmonary lesion.

5. The greatest case incidence is during the winter months.

6. There is no specific treatment. The sulphonamide drugs are not indicated.

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Bell: Introduction to carbohydrate biochemistry. 1943.
Canada. Department of National Defence: Physical standards and instructions for the medical examination of serving soldiers and recruits for the Canadian army, active and reserve. 1943.
Canadian Medical Association: Committee on economics. Health insurance; conference of Canadian health organizations. 1944.
Christopher: Minor surgery; 5th ed. 1944.
Clavero del Campo & Pérez Gallardo: Técnicas de laboratorio en el tifus exantemático. 1943.
Garrison: A medical bibliography. 1943.
Glasser: Medical physics. 1944.
Goodall: A study of endometriosis. 1943.
Grtnell and Hawes: Bibliography on lice and man with particular reference to wartime conditions. 1943. (Bibliographical bulletin No. 1.)
Halliday and Noble: Food chemistry and cookery. 1943.
Hamilton: Exploring the dangerous trades. 1943.
Harvey Cushing collection of books and manuscripts. 1943.
Hunt: Personality and the behavior disorders; 2v. 1944.
International Labor Office: The health of children in occupied Europe. 1943.
Jenkins and Hartung: The chemistry of organic medicinal products; 2d ed. 1943.
Landon: Lake Huron. 1944.
Lewin: Backache and sciatic neuritis. 1943.
Lowsley and Kirwin: Clinical urology; 2v. 1944.
*Freeman and Watts: Psychosurgery. 1942.
McQuarrie: The experiments of nature and other essays. 1944.
Manson-Bahr: Synopsis of tropical medicine. 1943.
Meakins: The practice of medicine; 4th ed. 1944.
Munroe: The training school for nurses, the Royal Victoria Hospital, 1894-1943. 1945.
Nash: Surgical physiology. 1942.
National Research Council of Canada: Abstracts on penicillin and other antibiotic substances. 1943.
Novak: Textbook of gynecology; 2d ed. 1944.
Peterson, Skinner & Strong. Elements of food biochemistry. 1943.
Pharmacopoeia of the United States of America, 12th revision; first supplement. 1943.
Recent progress in psychiatry. 1944. (J. Ment. Sc., v. 90. 1944.)
Ruiz: Relaciones entre las secreciones interna y externa del páncreas. 1936.
Salter: The endocrine function of iodine. 1940.
Sante: Roentgenological interpretation; 5th ed. 1944.
Seifert: Virus diseases in man, animal and plant. 1944.
Sigerist: Medicine and human welfare. 1941.
Tanner: Microbiology of foods; 2d ed. 1944.
Valentine: Experimental foundations of general psychology. 1943.
Voronoff: The sources of life. 1943.
Wharton: Gynecology, with a section on female urology. 1943.
Zilbooth: Mind, medicine and man. 1943.

PERIODICALS, ANNUALS, ETC.
American College of Surgeons: 1944 supplement to 1942-43 Yearbook.
American Laryngological, Rhinological, and Otological Society: Trans. v. 49. 1943.
Annual Review of Physiology: v. 6. 1944.
British Empire Cancer Campaign: Annual report. v. 20. 1943.
Chicago University, Douglas Smith Foundation for Medical Research: Studies. v. 15. 1942-43.
Inter-state Post Graduate Medical Association of North America: Proc. 1943.
National Foundation for Infantile Paralysis: Annual report. 1943.

The library staff wishes to express its appreciation to

(1) the physicians of London and district who responded so generously during the past few months to an appeal for their unwanted medical books and periodicals. These contributions are being used now for exchange purposes, or are being stored temporarily until such time as needed by libraries that have suffered loss during the war.

(2) the members of the Hippocratic Society who made possible the securing of much of this material by providing and manning a truck for their first office-to-office canvass.
A MEDICAL BIBLIOGRAPHY

A check-list of Texts illustrating the History of the Medical Sciences.


It was the late Sir William Osler who first suggested the need for such a work, and its usefulness was tried and proved by its original author, the late Dr. Fielding Garrison, in the research done in writing the “introduction to the History of Medicine”.

The revised edition in 1933 contained 4,186 items. In the 1943 edition, brought up to date by Leslie T. Morton, 360 of the original entries were omitted, while 1,680 new entries were made, bringing the total to more than 5,500.

The bibliography is arranged according to subjects and systems and the separate references under the headings are given in chronological order. An index of personal names and an index of subjects make the book readily usable.

Annotations added by Morton almost make the book a readable entity in itself. There is probably no other work in existence which will be as indispensable to medical libraries and historians.

—Ray Bainborough.

MEDICAL PHYSICS


This is the most energetic and optimistic work of its kind yet published. Physics has been used in the development of many medical techniques, but never before have the common meeting grounds of medicine and physics been gathered together and presented in one work with a threefold purpose of encyclopaedia, textbook and working instru-
ment “in which may be found the data necessary for actual employment of the principles of physics in medical practice”. In it are 255 articles by almost as many contributors, each an authority in his field. Twenty-three classified tables correlate all the contents. So great is the number and so diversified are the subjects that it is impossible to list here all the contents of this huge volume. Mention might be made, however, of such variegated subjects as air conditioning, aviation physiology, blood substitutes, enzymes, gait, growth, photography, tissue culture and repair and photochemistry.

A few of the great names that have come together in this work are William D. Coolidge (Coolidge X-ray tube), Robley D. Evans (artificial radioactivity), Harry Goldblatt (hypertension), E. Newton Harvey (luminescence), Chevalier Jackson (bronchoscopy), Matthew Luckiesh (Mazda Lamp), Clarence A. Mills (climatic effects), Robert S. Stone (cyclotron and neutron therapy), Hugh H. Young (Urology), and Vladimir Zworykin (television).

It would be too much to expect a work of this magnitude to be without shortcomings, particularly in the first edition, but the book has promise of going through many editions and time will iron out discrepancies and cull non-essentials from essentials.

—RAY BAINBOROUGH.

PHYSIOLOGY OF THE NERVOUS SYSTEM

By J. F. Fulton, M.A., D.Phil., D.Sc. (Oxon.), S.B., M.D. (Harv.), Sterling Professor of Physiology, Yale University.


This book comprises some 500 pages of recent conclusions on the function of the various parts of the nervous system. The fundamentals of nervous physiology are included for the benefit of the student, but the author in deference to the warring world has attempted to emphasize practical applications wherever possible. The reader’s attention is drawn to the significant recent developments: the very wide distribution along nerve fibres and their cells of acetylcholine and its enzyme cholinesterase and the importance of these substances not only in the metabolism of neurones but also in the development and propagation of the action potential; the interrelationship of parts of the cerebral cortex and ganglia; cerebellar functions, particularly in the primates; and the more accurate knowledge of the location of the respiratory centre.

Each subject is introduced with an historical note which recalls earlier important findings on the topic under consideration and a concise summary completes each chapter.

For obvious reasons a good deal of the information is based on
animal experiments but an interesting feature is the incorporation of detailed observations on four human cases with the following lesions:

1. Complete transection of the thoracic spinal cord.
2 and 3. Suprasellar cysts which, for physiological purposes resulted in decerebration. These two cases gave typical human decerebrate rigidity and Magnus and de Kleyn postural reflexes.
4. A tumour involving the hypothalamus with symptoms illustrating hypothalamic functions.

The bibliography is lengthy and shows a thorough recognition of the important work.

The book covers a very extensive field; both experimental and clinical observations are drawn from the work of the author and his students as well as from the researches of others. The style is clear and concise and of high literary merit.

—ELIZABETH FLECK.

SYNOPSIS OF TROPICAL MEDICINE

By Sir Philip Manson-Bahr, C.M.G., D.S.O., M.D., F.R.C.P.

Price, $2.50.

This synopsis is a guide in condensed form suitable for medical officers and the armed forces and others called to the tropics. It presents the geographical, aetiological, pathological, clinical and diagnostic features of a wide variety of diseases—protozoal, spirochaetal, rickettsial, bacterial, virus, fungus, nutritional and climatic. Included also are discussions of animal and vegetable poisons and simple laboratory methods for examination of blood, urine and faeces. A series of plates on parasites and protozoa complete the work. This book appears practical and useful and in its brief, condensed yet fully adequate presentation is very appealing.

—C. B. CANTELON.

CONTEMPORARY PSYCHOPATHOLOGY

Edited by Silvan S. Tomkins, Ph.D., Instructor in Psychology
Harvard University.

This collection of modern psychological papers had been designed as a source book for courses in abnormal psychology. It serves to bridge the gap between the student and the voluminous periodical literature. The contributing authors have treated psychopathological conditions not so much descriptively as with reference to origin and dynamics.

The papers are arranged under four headings, as follows:
1. **MENTAL DISEASE IN CHILDHOOD** (7 papers).

Disorganizing factors affecting the developing personality of the child are pointed out. The importance of infant suckling is stressed in relation to reflex stimulation of respiration and the development of the higher associative faculties.

A paper entitled “Release Therapy” deals with the study of the child’s play in reference to the solution of his emotional difficulties.

2. **PSYCHONEUROSIS AND PSYCHOSOMATIC MEDICINE** (10 papers).

The close relationship between gastro-intestinal disturbances, repressed desires and anxiety is pointed out.

The mechanism, symptoms and treatment of “traumatic neurosis” is described in a paper entitled “The Neuroses of War”. Traumatic neurosis is found to differ considerably from the hysterical neurosis precipitated by trauma.

An interesting relationship is established between bronchial asthma and psychology. Asthma would seem to have an emotional as well as an allergic origin.

3. **THE SCHIZOPHRENIC PSYCHOSES** (13 papers).

Schizophrenia is shown not only to be a psychologic withdrawal but also a reduction of physiological activity. Which is cause and which effect is not certain.

An analysis of the insulin and metrazol treatments is given and a comparison drawn.

Prefrontal lobotomy is discussed and shown to result in a reduction of the consciousness of self and an outward turning of the patient’s interest.

An interesting study is reported of two schizophrenic patients who recovered. An acute psychosis may be a transitional episode in the changing over from an outgrown method of adjustment to a more adult behaviour.

4. **EXPERIMENTAL PSYCHOPATHOLOGY** (15 papers).

Experiments with rats show that under competitive conditions recently learned responses disintegrate and the rat regresses to previously conditioned responses.

Work with dogs shows that “nervous disturbances” can be developed by conflicting situations. The symptoms can be relieved by rest in a change of environment but not in the environment of the experiment.

An interesting paper on hypnotism proposes the theory that hypnotic behaviour represents goal-directed striving. The subject is ruled by the wish to behave like a hypnotized person, i.e., to obey the instructions of the operator. This behaviour is the goal toward which the subject strives.

The book will be found instructive by those interested in the psychosomatic aspects of medicine.

—KEN WARD.
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