The Treatment of Chronic Liver Disease

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THE evaluation of the results of a single therapeutic measure in chronic liver disease is difficult for two reasons. First, it is almost impossible to provide only one therapeutic agent at a time, and second, the course and prognosis in chronic liver disease are so variable that controlled observations can seldom be made. The therapeutic recommendations reported here are derived in part from the work of others, to which the reader is referred from the original data, and in part from our own work in progress which is largely uncompleted and should be considered as suggestive rather than conclusive.

Although one or more specific etiologic factors may be responsible for the eventual production of chronic liver disease, all lead to a similar clinical and pathologic entity covered by the term cirrhosis, with attendant decrease in the number of functioning liver cells and pronounced increase in fibrous tissue. Among the known or suspected causes of cirrhosis one may list: inadequate or faulty nutrition, which is often associated with chronic alcoholism; chemical toxins, especially the chlorinated hydrocarbons and arsenic; infectious hepatitis\(^1\),\(^2\),\(^3\),\(^4\) and "cholangiolytic hepatitis";\(^5\) chronic biliary obstruction; and perhaps certain specific infections such as brucellosis.\(^6\)

A few characteristic syndromes may usually be seen in these instances of chronic liver disease, whether arising from deficiencies,

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from toxic or infective agents, or from other sources. In the first place there may be anorexia, loss of weight and similar complaints indicating either poor digestion and absorption or perhaps a deficient ability of the liver to conduct its metabolic functions: Secondly, a diminished excretion of bilirubin and urobilinogen may be observed, followed by a rise in the serum bilirubin, the appearance of clinical jaundice, bilirubinuria and an increased urinary excretion of urobilinogen. The third syndrome usually arises when far advanced fibrosis is present, and is characterized by the appearance of ascites—often with dependent edema. Esophageal varices which may develop in patients with chronic hepatic fibrosis sometimes rupture with resolute massive acute blood loss and frequent exodus. Finally, the ill-defined but clinically easily recognized “liver coma” or “cholemia” is to be mentioned. It should be understood that each of these syndromes is not necessarily separable from the others. A given patient may show any of a group of signs or symptoms related to one or more of the syndromes mentioned. Generally, however, one syndrome predominates in each individual. It will not be possible in this paper to discuss the other signs and symptoms and the laboratory tests which help in establishing the diagnosis and in assessing the severity of chronic liver disease. In this regard the reader is referred to several recent papers.7,8,11

The greatest advance in the treatment of chronic liver disease in modern times was that described in 1941 by Patek and Post10. The title of their paper, “Treatment of Cirrhosis of the Liver by a Nutritious Diet and Supplements Rich in the Vitamin B Complex”, places the emphasis where it belongs, upon the diet and its nutritious and adequate nature and not as some have mistakenly supposed upon the Vitamin B complex alone. The diet described by these workers was relatively high in calories, protein and fat.

The rôle of protein in the diet is somewhat difficult to define. Work in experimental animals for a number of years has shown that diets grossly deficient in protein may lead to hepatic disease,12,13,14 but it has not been demonstrated either in man or animals that a diet containing more protein than is adequate for the normal individual hastens recovery. Nevertheless, it has become customary and is perhaps safer to provide fairly large amounts of protein in the diet of patients suffering from chronic liver disease. For the normal adult individual 1 gram of protein per kilogram of body weight is usually considered adequate, but in patients with cirrhosis this amount should be increased to 1½ to 2 grams per kilogram per day.

Experimental work in animals has suggested that the protective and curative effect of dietary protein for the liver resides in part in its content of sulfur containing amino acids, especially methionine, perhaps because of the ability of this amino acid to donate methyl
groups for the synthesis of choline.\textsuperscript{14,15} In the absence of sufficient choline or methionine, fatty changes occur in the liver of experimental animals and fibrosis may follow. When these and perhaps other "lipotropic" substances are added to the animals' diet the fat disappears and the liver returns to normal. There is no well controlled study in man indicating that any one or more of these substances is beneficial above the amounts to be found in a "nutritious diet".\textsuperscript{16} There is still a considerable amount of discussion concerning the kind of protein to be included in the diet. Some earlier work with experimental animals led to the belief that animal protein, particularly red meat, was damaging to the liver.\textsuperscript{17} There is, however, little if any clinical evidence that animal protein is damaging to the human liver, diseased or not, and thus at the present time in most clinics it has become the custom to provide the protein in that proportion from animal and vegetable sources found in the usual nutritious diet. It should not be forgotten that vegetables, milk, eggs and cheese, as well as meat, are important sources of very good protein.

The injurious effects of fat in the treatment of chronic liver disease have been over-emphasized for many years. It is true that in animals on a protein-deficient diet containing large amounts of fat that fatty changes may occur in the liver,\textsuperscript{18,19} but this does not occur when the protein content of the diet is adequate; even though the fat content may be relatively high. Patients with complete or almost complete biliary obstruction are unable to tolerate fat in the diet very well, presumably because of poor fat digestion in the absence of bile in the gastro-intestinal tract. Individuals with chronic liver disease, however, rarely have severe biliary obstruction and are able to digest and absorb fats. Moreover, a low fat diet is difficult to prepare and unappetizing, and as it is of the utmost importance to entice patients with liver disease to eat well, fat in moderate amounts is certainly indicated. Finally, the diet with which Patek and Post achieved such good results contained roughly 175 grams of fat per day, indicating the harmlessness and therapeutic value of a diet ample in fat.

In the presence of anorexia it is often difficult to convince both the patient and his attendants that food is the "medicine" of choice and that it must be eaten. In order to assure an adequate intake of important nutrients, food supplements are prescribed for patients with chronic liver disease. These are often taken by patients almost as a medicine when food is refused and frequently, in fact, increase the appetite so that more food is eaten. Brewer's yeast is most commonly used but must be given in amounts of 30 to 45 grams per day,\textsuperscript{10} mixed with water, milk, or into an eggnog. We have had some experience with a liver protein mixture which is nutritious and fairly well taken by most patients with chronic liver disease.\textsuperscript{20}
The parenteral use of a crude liver extract has long been recommended in the treatment of chronic liver disease. For the reason that large amounts of liver extract cannot conveniently be given intramuscularly, the intravenous route has been chosen by some and has recently been described as an adjunctive therapeutic measure by Labby et al. Our experience with intravenous crude liver extract in large amounts for prolonged periods of time, two or three months of daily administration, has led us to conclude that the material produces a dramatic therapeutic result in only very occasional patients.

If the patient cannot eat the requisite amount of food, other food supplements, in addition to liver extract, may, of course, be administered intravenously. Glucose may be given in large quantities, a 15 per cent solution being advantageous. Protein hydrolysates are well tolerated intravenously in liver disease and furnish protein building materials.

The treatment of ascites and edema in chronic liver disease presents a special and important problem. Paracentesis abdominis has been performed since ancient times for the relief of ascites, but in most cases is purely palliative and must be repeated over and over again until a fatal termination ensues. Paracentesis is indicated only if the amount of ascites present interferes with body functions, resulting in dyspnea or decrease in the patient's appetite and ability to ingest good food in reasonably adequate amounts. A low sodium diet may help prevent the reaccumulation of edema and ascites in some instances. It is, however, quite difficult to prepare a palatable and adequate diet with less than 1 gram of salt per day. With the patient's co-operation a low sodium diet should be tried, however. A low sodium milk powder is available and is an excellent means of furnishing protein as well as carbohydrate to these individuals. For discussion of the components of a low sodium diet the reader is referred to recent papers.

Among the diuretics, ammonium chloride and the mercurials have received the widest acceptance. The response is, however, exceedingly variable and one should not count on it as more than a therapeutic adjunct in the case of water retention in chronic hepatic disease. Nevertheless, repeated injections of a mercurial diuretic at regular intervals may be sufficiently effective to hold the ascites and edema in check for many months.

Recently the administration of normal human serum albumin has been recommended in the treatment of ascites and edema in patients with chronic hepatic disease. This material, prepared during World

**"Intraheptol", Lederle Laboratories Division, American Cyanamid Company, New York, N.Y.**

**"Lonalac", Mead Johnson & Co., Evansville, Indiana.**
War II for use in the treatment of shock\textsuperscript{25,26} has been found, because of its slow \textit{in vivo} degradation,\textsuperscript{27} to be of value in raising the serum albumin concentration when administered intravenously in relatively large amounts to patients with cirrhosis. It is believed that the ascitic and edema fluid is mobilized for excretion by the rise in colloid osmotic pressure resulting from the rise in serum albumin concentration. The best responses are found in patients with marked edema accompanying their ascites, the poorest in patients without edema who require frequent taps to control their ascites. Nevertheless, even a few patients of the latter category may respond to the prolonged administration of albumin intravenously when the serum albumin concentration is in this way maintained at normal. While there is no question but that the use of albumin intravenously in patients with chronic liver disease with ascites and edema is a definite therapeutic advance, caution must be observed in placing too much reliance or enthusiastic approval on this method of treatment until a large series of patients have been treated and presented together with proper controls. At the present time very little normal human serum albumin is available on the market, and its expense is almost prohibitive. It is to be hoped that this situation may change as the usefulness of albumin becomes more widely known.

The treatment of massive hemorrhage from bleeding esophageal varices has always been a difficult problem. With the advent of the modern blood bank and the easy availability of whole blood as well as of blood derivatives for the treatment of shock from acute blood loss, many lives have been saved. The various surgical procedures which have been suggested for the removal or obliteration of esophageal varices\textsuperscript{28,29} and for the shunting of blood from the portal bed to the systematic circulation\textsuperscript{30,31} will not be discussed here. The results of these procedures are too recent to permit proper evaluation, but they should certainly be considered in patients with chronic liver disease in whom esophageal varices are found, particularly after one bleeding episode has occurred.

Patients with chronic liver disease have a proclivity to develop coma. Usually it develops gradually over a period of 24 hours or so and is characterized by lack of significant new or changed physical or biochemical findings. Very little hint as to the etiology of “liver coma” or “cholemia” has been found. Nevertheless, three factors, the injudicious use of sedatives and analgesics, the presence of severe acute infection and the occurrence of gastrointestinal hemorrhage have been shown to be etiological factors in a majority of patients.\textsuperscript{82}

Although not widely known, it has been demonstrated that most sedatives are very poorly tolerated in patients with severe liver disease and their injudicious use may lead to irreversible coma. The classical
example is morphine, which even in small doses has a much more marked and prolonged effect than in patients without liver disease. This is also true of codeine, although to a less extent, and of some of the other morphine and opium derivatives and of the barbiturates as well. Paraldehyde, often prescribed in liver disease because of its supposed innocuousness, should also be used with great care. In fact, the problem of the proper treatment of an excited patient with liver disease is a very difficult one. It may be that some of the sedatives that are largely excreted in the urine, such as barbital and, to a less extent, phenobarbital, may be better tolerated in liver disease than those destroyed or excreted by the liver.

The effect of infection upon the liver has not been critically studied. Nevertheless, it is quite clear that patients with severe infections may develop temporary impairment of liver function and that patients with liver disease may have an exacerbation thereof because of severe infection. In fact, in patients with liver disease, coma may be precipitated by such severe acute infections as pneumonia, endocarditis, meningitis, etc. In these instances, of course, the treatment is directed first to the acute infection itself by use of chemotherapeutic agents. Acute blood loss, usually from bleeding esophageal varices, with anemic anoxia and shock, frequently leads to coma, and is best treated, of course, with prompt whole blood transfusions.

Analeptics and convulsants have little effect in liver coma. If the coma arises spontaneously, that is, without contributory sedative administration, acute blood loss or infection, the prognosis is extremely poor. If one of these complicating or initiating factors is present and is susceptible to treatment, a few such patients may recover. Thus, apart from the administration of blood or specific chemotherapeutic agents, therapy in liver coma is directed at maintaining good nursing care, preventing bronchopneumonia and aspiration pneumonia, administering fluid in adequate amounts to assure a reasonable urinary output, and maintaining nutrition by either tube feedings or intravenous feedings, or a combination of both. Intravenously one may administer glucose in large amounts, sodium chloride as needed, vitamins and liver extract. Protein is best supplied as a protein hydrolysate and is well tolerated in most individuals with liver coma.

**SUMMARY**

In briefly reviewing the therapeutic measures available for the treatment of chronic liver disease, it is first emphasized that the results of any therapy are difficult to evaluate because control observations are seldom available.

Therapy in chronic liver disease is based upon the fundamental principle of insuring that nutritious food is eaten, digested, and ab-
sorbed. The diet must provide 1 to 2 grams of protein per kilo of body weight per day. To be palatable and adequate in calories it should not be restricted in fat content. Substances such as methionine and choline are present in considerable quantities in such diets and have not been shown to be necessary as supplements. Crude food supplements, however, such as brewer's yeast, may stimulate the appetite and at the same time act as a further source of nutrients. Crude liver extracts prepared for intravenous use rarely cause striking therapeutic benefits and then apparently only as a result of increase in appetite and food intake.

Ascites and edema in chronic liver disease respond in some instances to the simultaneous use of a low sodium diet, diuretics, and the artificial increase in the serum albumin concentration by the intravenous administration of salt from normal human serum albumin.

In the prevention of "liver coma" emphasis is placed on the careful use of sedatives and the prompt treatment of infections and of blood loss. Treatment of this poorly defined condition is supportive only and must provide adequate fluid and food intake either orally, by stomach tube, or parenterally.

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Head Injuries

By James Machan, '48

I. Introduction

The field of head injuries is vast and fertile. In this one great arena we find at work specialists from nearly every branch of medicine. The work of the surgeon and the neurologist is obvious. The pathologist is as ever hard at work here, laying the foundation stones of our knowledge wherever we go. We find at work with these men, the psychiatrists who have a special interest in the prevention and care of the neuroses which tend to follow head injuries. Here too is represented the obstetrician and pediatrician who are especially concerned with birth injuries. Also we can meet with such men as radiologists and specialists in industrial medicine. And perhaps most important of all is the general practitioner to whose lot often falls the initial recognition and handling of all types of head injuries.

With such a vast subject it is necessary to limit oneself to a small portion. I wish to discuss in particular the various aspects of "closed injuries of the head". This means that the brain has not been penetrated by a missile and that a compound fracture of the vault has not occurred. At all times no attempt is made to trespass into the dense jungle of detailed pathological descriptions, advanced methods of diagnosis or complex surgical treatment, though these are of great importance.

II. Mechanism of Injury

Here we must consider the injury which may occur to the skull and secondly the injury which may occur to the brain.

A. Fracture of the Skull: Bone possesses the property of elasticity. It will bend whenever a force of sufficient magnitude is applied to it. Whether it breaks depends on the degree of bending. Bending is certainly the means by which most fractures of the skull are produced, and the injuring force may act (1) by deforming a circumscribed area of bone, or (2) by distorting the shape of the skull as a whole. The exact manner in which the bone breaks is determined by the fact that the tensile strength is less than its power to resist compression. Therefore the table of bone on the convexity of the bend, and thus subjected to stretch, will be the one to fracture first.

(1) Fracture due to local deformity: This type is caused by some small mass striking the head squarely. This mass will cause a cone-like indentation of the bone. At the apex of such a cone the inner table will be stretched whereas the outer table will be compressed. Thus
the inner table fractures first. Fracture of the outer table follows as the force continues to act. At the periphery the reverse process occurs.

(2) Fracture due to general deformity: The skull behaves as an elastic sphere. Thus, if it could be dropped it would rebound, owing to a temporary change in shape. A force applied to any point on its surface must cause not only that point, or pole, of impact to be flattened but the opposite pole as well. In the formation, the skull (or sphere) expands at the equator. Such a force is equivalent to compression of the skull between two fixed points. If the resultant change in shape is great enough the skull will crack in the direction of a meridian of longitude, that is, from pole to pole. If the skull were a sphere or an ovoid body with a shell of uniform thickness, the line of fracture would take exactly this course. But the skull is not of uniform thickness; its bases have definite buttresses with weak areas between them; namely the posterior, temporal and frontal fossae. Thus the fissure is usually found in one of these weak areas at the base commonly in the temporal fossa.

The main significance of the fractured skull lies not in the fact that the continuity of the bone has been broken, but that the fractured skull indicates that serious underlying damage may have occurred as a result of a force great enough to fracture the skull.

B. Injuries of the Brain: Apart from penetrating wounds of the skull (which as stated above do not form the major part of our discussion), the brain can be injured in one of two ways: (1) by movements of the brain within the skull, or (2) by distortions of the skull. In the adult where sutures are firmly closed and the bone brittle by calcification any distortion of the skull sufficient to cause injury to the brain is usually sufficient to cause a fracture.

(1) Movements of the Brain Within the Skull: When a man is thrown on his head against some resisting object, the skull at some phase of the injury becomes stationary, whereas the brain, in virtue of its momentum and the fact that it does not completely fill the cranial cavity, travels onward in the direction thrown and is injured by the forces which resist its movement and finally bring it to rest.

The advancing brain comes into forceful impact with segments of the skull or with the face or edges of the dural septa. Because of their firm attachment to the bone and their rigidity, the dural septa act as part of the skull in resisting the movements of the brain.

Example One: In lateral movements of the brain within the skull the following will occur: the outer surface of one hemisphere strikes the side of the skull, whereas the inner surface of the opposite
hemisphere strikes the flat surface of the falx; the brain stem impinges against the edge of the tentorium and one side of the cerebellum strikes the lateral wall of the posterior fossa.

Example Two: When the brain is thrown away from the base of the skull, the upper halves of the outer surfaces of the cerebral hemispheres strike the vault of the skull; the upper surface of the corpus callosum strikes the free edge of the falx cerebri; the upper surface of the cerebellar hemispheres is pressed against the under surface of the tentorium cerebelli.

As a result of this movement of the brain within the skull the following injuries are possible: (a) Injuries by impaction such as contusion and laceration (which will be discussed in detail below).

(b) Injuries by suction. At the pole opposite to the site of impact the brain moves away from the skull and before the space produced can be filled with cerebral spinal fluid a zone of diminished pressure results in which suction may be sufficient not only to rupture surface vessels but also vessels more deeply placed.

(c) Rupture of vessels by stretching. The mere sliding of the brain within its dural coverings is a very serious matter for not only does it account for the rupture of tethered surface blood vessels but also for the avulsion of cranial nerves.

The vessels which drain the cortical veins are especially susceptible to rupture as they cross the subdural and subarachnoid spaces because they have thin delicate walls and because their course is short and straight and the two extremities of the vessel are firmly fixed. This event accounts for most of the cases of profuse subdural and subarachnoid haemorrhages. The arteries at the base of the brain are rarely subjected to such an injury because they run a tortuous course. Therefore, they can take up a good deal of slack before they become taut. Also their walls are thick and strong.

(d) The brain is not a homogeneous body of uniform consistency. It is composed of tissues of differing densities (white and gray matter). Moreover the brain does not act as a single unit. Each hemisphere is separated from the other except for its connection with the corpus callosum. Also both hemispheres are connected with the cerebellum only through narrow pathways of the brain stem. This means that large anatomical units can move in relation with each other and that the whole brain can move in relation to the skull. Thus connecting pathways may easily be bent, stretched or torn wherever the brain is made to alter its shape. It should be noted here that the cushion-like action of the cerebral spinal fluid tends to minimize these four types of injuries.
(2) Distortions of the Skull: In distortions of the skull there is a lag in the moulding of the intracranial contents to the new curvature of the bone, so that parts of the brain can be subjected to either increased pressure or suction. Also, as the skull rebounds after the injuring force has ceased to act, important structures may be torn; and in particular, if the dura does not allow the movements of the skull, the meningeal vessels will be pulled away from the bone and small nutrient vessels broken. Rupture of the main vessels depends upon certain peculiarities. Often the vessels are imbedded in a deep bony groove with overhanging edges in the proximal part of their course; whereas from the Sylvian point onwards they are firmly attached to the dura and therefore will break at this point of junction whenever the skull moves away from the dura. This is an important cause of extra dural haemorrhage.

At this point it will be advantageous to mention the term, injury by "contre coup". It is used in a sense that a pole of the brain opposite to the site of impact has been damaged. Often this damage is the most serious incurred by the brain.

III. PATHOLOGY

The importance of the pathology of brain injury for intelligent diagnosis and judicious treatment cannot be overstressed. The subject is, in some aspects, by no means clear. These controversial points will be noted in passing.

One feature of brain trauma which must be stressed is that in every case of brain injury, even in a moderately severe one, pathological changes will be found not only in the tissue directly affected by the trauma, but also in regions remote from the local injury. Histological changes in cerebral trauma then are both local and diffuse. Although in some cases the local changes may appear insignificant, the diffuse changes may be profound. I wish to stress again that we are talking here entirely of closed injuries of the brain. For simplicity and clarity let us divide our pathological states into Primary Pathological states and Secondary states.

A. Primary Pathological States: During the few moments the accidental forces are operating the brain can be damaged in three and in only three ways. It may be contused; it may be lacerated; or, its neurons may undergo a diffuse injury of submacroscopical dimensions (this is called concussion). One or any combination of these conditions may occur. All other phenomena such as oedema and massive haemorrhage are secondary.

I. Contusions:

Cerebral contusions are microscopic solutions of continuity of
brain tissue. They may occur on the surface of the brain or deep within its substance. Both types are necessarily associated with bleeding though this is usually punctate and limited to the area of the bruise. When superficial they are seen as sub-pial gelatinous-looking stains of a mottled reddish-blue color covered by a thin layer of blood. Thick clots cannot occur because the pia is firmly attached to the brain tissue and will not readily strip. Often contusions are wedge-shaped with the apex of the wedge extending into the cerebral tissue for a distance of 1-2 cms. but rarely deeper than this. Contusions may be single or multiple; more than one surface of the brain may be involved. They may be no larger than a pinhead or they may cover large areas on both sides of the brain. Within the brain substance contusions are seen as clusters of petechial haemorrhages superimposed on a dull gray background. Most commonly they occur in the white matter of the hemispheres, but they are also found in the cerebellum, medulla, pons, midbrain, thalamus, hypothalamus, caudate nucleus, lenticular nucleus and in the sub-ependymal layer of the ventricles and of the aqueduct of Sylvius. They may be single or widespread.

The microscopic picture shows either superficial or deeply-placed contusions as spots or streaks of extravasated blood surrounded by an area of damaged brain cells, beyond which is a zone of oedema. The extravasated blood is due either to rupture of blood vessels or to diapedesis. The area of damaged brain cells is composed of three concentric zones, each one being distinguishable from the other by the nature of the cellular changes within them. Nearest to the extravasated blood, the neurons, glial and microglial cells are completely destroyed and often in a state of liquefaction. In the middle zone the staining properties and the shape of the cells is altered in such a way that it is impossible to know whether the cells have been damaged permanently or not. At the periphery, the neuroglia, astrocytes and microglia are hypertrophied and increased in number, and it is from this zone of increased cellular activity that the process of phagocytosis and repair are initiated. Many of the cells within a contusion, though functionally paralyzed, are viable and will recover under favourable conditions or will succumb if the cerebral circulation is impaired by secondary developments such as oedema.

II. Lacerations:

Lacerations are gross solutions of continuity of brain tissue. They differ from contusions merely in their severity. Most commonly they are found on the under surface of the frontal lobes and near the tip of the temporal poles. Usually they are superficial but they may be deep enough to open into a ventricle or cut across a basal nucleus such as the hypothalamus. The pia is invariably torn. So the ruptured cortical vessels may bleed with little restriction into the voluminous
sub-arachnoid space. Tearing of the arachnoid allows blood and C.S.F. into the sub-dural space. The tough dura rarely gives way.

III. Diffuse Neuronal Injury:

Another term commonly used here is concussion. The whole subject of concussion is complex and controversial.

Contusions, lacerations and haemorrhage commonly found at autopsy or on surgical exploration after a head injury, often will not account for the unconsciousness with its allied neurological states. Therefore, cells or pathways concerned in the initiation or transmission of nervous impulses, other than those in the areas which have undergone damage of macroscopical dimensions, must have been affected by the injury. But just how the cells or pathways have been affected is the question not yet settled.

According to one theory, the cerebral anemia, resultant on the injury, gives rise to the unconsciousness—the state of concussion. Others will maintain that the cause of concussion is a molecular derangement of the neurons—as though the neurons, jarred by the blow, are so severely shaken up that their connections one with the other, are disturbed and so they can no longer transmit impulses and unconsciousness ensues. This has been called commitio cerebri or commotion of the brain cells. However, a more logical theory is that concussion is based on a direct diffusely scattered injury of an organic type due to a large number of neurons.

B. Secondary Pathological States:

The moment of impact determines the primary pathological events. If that part of the brain which is essential for life has not been destroyed by these events the natural tendency of the patient is towards recovery. This recovery is, however, impaired by the secondary pathological changes, some of which, unfortunately, invariably occur.

The secondary pathological states include the following: (1) Shock, (2) Massive haemorrhage, (3) Oedema, (4) Hydrocephalus, (5) Herniation of the brain, (6) Meningitis and Encephalitis.

Let us discuss each of these in turn.

(1) Shock: Immediately after the injury we often see a state of primary shock. This is a condition of collapse which may follow soon after the receipt of an injury and which is not due to the loss of blood. It responds rapidly to warmth, rest and relief of pain.

Secondary shock is a condition of circulatory failure. It develops insidiously some hours after the injury and may be induced by haemorrhage, cold, pain or toxins. Although we are discussing closed head injuries, the loss of blood even here is considerable. This may occur from nose, ears, cuts on scalp, into sub-glial tissue and into the sub-arachnoid...
space, or from wounds elsewhere in the body. The cold often results from exposure. Pain induces shock itself and also causes restlessness leading to exhaustion which aggravates the state of shock. Toxic absorption from broken-down tissue proteins may occur.

The picture of shock in the conscious patient is obvious, but in the unconscious patient cannot be distinguished from a deteriorating state of concussion.

(2) Massive Haemorrhage: Massive haemorrhage following head injury can readily be divided into two types: (a) Extra-dural, and (b) Sub-dural Haemorrhage.

(a) Extra-dural haemorrhage—large enough to be of surgical significance is very rare, constituting about \( \frac{1}{2} \% \) of cases of acute cerebral trauma. These cases are, nevertheless, very important. The source of bleeding may be from three possible sources: 1. Middle meningeal artery. 2. Diploic veins. 3. Dural venous sinuses.

In an analysis of 25 cases of extra-dural haemorrhage: 15 were middle meningeal, 6 were due to bleeding from diploic veins and 4 from tears in the wall of dural venous sinuses.

Haemorrhage from the middle meningeal artery, being the most common, is the only one which we will describe. The vessel may be ruptured in many ways. It may be transfixed by a spicule of bone or lacerated by the edges of a fracture or it may be torn by stretching. Bleeding may not take place immediately when the vessels are torn due to the influence of shock. But, as the circulation recovers and the blood pressure rises, rapid and profuse bleeding may occur. The latent interval which so commonly occurs in middle meningeal haemorrhage is not always due to shock but often can be accounted for by the ability of the brain to accommodate itself to a slowly expanding lesion for a long time before showing signs of compression. In many cases the vessel bleeds from the moment of injury but often at a slow rate, due partly to incomplete rupture and partly to the resistance of the dura to stripping. Immediate prodromal symptoms such as headache are the rule rather than the exception and the rapid development of neurological signs indicate loss of compensation in the brain rather than a sudden severe haemorrhage.

(b) Sub-dural haemorrhages—The arachnoid and dura, though normally lying in close contact with one another, are readily separable and enclose a potentially large space which can be converted into an extensive cavity by haemorrhage or leakage of C.S.F. Bleeding into the sub-dural space results usually from a dural venous sinus. If the arachnoid has been torn it may come from a cortical vein. Most commonly it is from short communicating veins which drain the cortical veins into the sinuses.
Though not common the bleeding on occasion may be profuse, giving rise to an acute sub-dural haematoma.

When we have lacerations of the arachnoid, C.S.F. is allowed to escape into the sub-dural space giving rise under the proper conditions to a massive collection of fluid in the sub-dural space—an Acute Sub-dural Hygroma.

The condition, however, with which we are all familiar and which has received more study is the Chronic Sub-Dural Haematoma. Though again this condition is rare, comprising less than 1% of cases, it is of extreme interest because of the manner of its development and the excellent results obtained by proper treatment.

The condition may arise following only a very slight knock on the head. A vessel, probably a vein, ruptures and then seals; and the resulting haematoma becomes enveloped in a fibrinous membrane which later is organized by mesothelial invasion. The part of the membrane nearest the arachnoid remains thin and non-adherent, whereas the outer part thickens and becomes attached to the dura and is impossible to strip without rupturing numerous small blood vessels (a point of surgical significance). At some phase in its life history the clot begins to swell, but why this happens is uncertain. Since it has been proven that the membrane of the haematoma is semi-permeable, it is logical to assume that as the clot disintegrates, its molecular concentration will increase and cause a rise in osmotic pressure, with the result the C.S.F. will be drawn through the semi-permeable membrane by the process of dialysis. This, however, is only one theory and there are other theories to explain the mechanism.

Sub-arachnoid bleeding:

This is by far the most important and the most common form of massive bleeding due to acute cerebral trauma. It is found in at least 75% of patients who have been unconscious for over one hour.

The bleeding may come from any vessel on any surface of the brain. If the haemorrhage is profuse it usually comes from a communicating vein of a dural venous sinus. The blood collects chiefly in the sulci, which it appears to fill. It also mixes freely with the C.S.F. which prevents its clotting. The presence of blood in the sub-arachnoid space is revealed by lumbar puncture.

The following are a few points which indicate that the blood is from the sub-arachnoid space:

(1) An even admixture of blood which is the same in a series of specimens collected from the same puncture. It is usual to collect three samples of C.S.F. in separate test tubes. These can be compared: if the amount of blood is the same in each it means that blood is
from the sub-arachnoid space. If the amount of blood is greater in
the first test tube collected; much less in the second, and almost absent
in the third needle trauma is indicated.

(2) Absence of coagulation.

(3) Pink, brown or yellowish coloration of the clear supernatant
fluid when the red cells have been allowed to sink to the bottom of the
test tube.

The irritation of blood in the meninges, when superimposed on
the effects of primary injury, is extremely serious. It causes, for
instance, restlessness of the patient. This restlessness causes cerebral
congestion. The congestion may cause increased bleeding or precipitate
cerebral oedema. Blood loss may cause anemia. Large quantities of
extravasated blood have the compressive effect of a large clot. Also,
resulting meningeal adhesions lead to faulty circulation and absorp-
tion of C.S.F.

Other forms of bleeding which are less common are: sub-pial,
 intra-cerebral and intra-ventricular.

(3) Oedema: When we come to the consideration of cerebral
 oedema we find various opinions. About this factor revolves a major
portion of our rationale in the treatment of cerebral injuries, as will
be pointed out later.

The American school, headed by such celebrities of cerebral injury
as Fay and Munro, believe oedema to be a very important and universal
occurrence following cerebral injury. The British and Canadian schools
do not, however, believe oedema to be nearly so important.

Cerebral oedema implies that the brain is swollen, owing to
increased fluid in the peri-cellular and peri-vascular
spaces. It does
not refer especially to the amount of fluid in the cerebro-spinal space,
although this reservoir will necessarily be increased. The histological
picture of this condition is typical, the tissue appearing areolar and
honey-combed due to distention of the spaces mentioned above.

The cause of the oedema is in question by both schools. One
thought is that it is due to an increased secretion of C.S.F. by the
choroid plexus. Another is that it is due to increased capillary perme-
ability consequent upon abnormal metabolites in the interstitial spaces,
or on vasomotor paralysis in the region of the brain concerned. When
the condition of oedema has developed, venous congestion will tend to
perpetuate it. In fact a vicious cycle results. Oedema leads to increased
intracranial tension; this causes venous congestion, and the venous
congestion, by causing further capillary stasis, increases the oedema.

That cerebral oedema always occurs locally about the area of
contusion or laceration is agreed on by all. Also, that generalized
cerebral oedema can occur is agreed on by all. Where the difference of opinion exists is that the American school claims the generalized oedema is a usual occurrence in acute cerebral trauma; the British and Canadian schools, on the other hand, feel that generalized cerebral oedema is not very common and its importance greatly over-emphasized. This disagreement influences to a considerable extent our form of treatment to be taken up later. It is a quantitative rather than a qualitative disagreement—physiological rather than pathological.

(4) Hydrocephalus: This is another secondary pathological manifestation. There are two types of hydrocephalus: internal and external. Internal, where there is some blockage in the ventricular pathway, is rare in acute cerebral trauma. External hydrocephalus, where the C.S.F. can leave the ventricular system and pass into the sub-arachnoid space, is more common in acute cerebral trauma. The causes may be: (1) excessive secretion, (2) faulty absorption and (3) obstruction to the circulation of the C.S.F.; or a combination of these factors.

Excessive secretion follows some trauma to the choroid plexus. Blockage of the arachnoid villi by extravasated red cells will cause blockage of absorption. Interference with the circulation by blood clots or adhesions will cause hydrocephalus. The hydrocephalus will cause signs of cerebral compression just as will a sub-dural haematoma.

(5) Herniation of the brain: Whenever the brain swells or whenever the intracranial space is encroached upon by an expanding lesion, such as an extra-dural haematoma, C.S.F. is forced into the spinal theca. Later the basal cisterns are obliterated and the ventricles become flattened. If the forces of compression or of oedema continue to act beyond the limits within which compensation is possible by further expulsion of C.S.F. or of blood from the intracranial cavity, processes of brain tissue are apt to be forced through the openings of the hiatus tentorii or of the foramen magnum as elongated herniations.

Tentorial Pressure Cone: The tentorial pressure cone is a most important complication. During some phase of the rise in supratentorial pressure a process of brain tissue from the under and inner surface of the temporal lobe (uncus) is herniated through the opening of the tentorium. The midbrain is displaced and compressed against the opposite free edge of the tentorium or, if the herniation is bilateral, between the two hernial processes. As a result, conduction of impulses from the cerebrum is impaired and the neural mechanisms below the compression are released from the control of higher centres. It is as if the brain stem were severed at this level. This gives rise to the state of decerebrate rigidity which follows experimental transection of the brain below the red nucleus.
Another important complication is that the third cranial nerve may be stretched or compressed by the herniation. It is this mechanism which accounts for a most important diagnostic sign, viz: the fixed dilated pupil. If not relieved, tentorial compression soon leads to death in coma.

*Cerebellar Pressure Cone:* A rise in pressure in the posterior fossa may force the tonsils of the cerebellum through the foramen magnum into the spinal canal with resulting compression of the medulla oblongata. This compression leads to respiratory embarrassment which might go on to complete failure. Although the circulatory centres may continue to function for some time, sooner or later they also fail and the patient dies.


This, then, is the pathological picture. Each phase has been given considerable prominence. It remains finally to place these various and varied pathological changes into their proper perspective. We thus can form a picture of what usually occurs following cerebral trauma.

The initial injury can produce one of any combination of three pathological states: contusion, laceration or concussion. If these damage the brain stem and the basal ganglia that are essential to life, all is lost. However, if these are spared so that respiration and circulation adequate for life continue, the natural tendency is towards recovery.

The extent and degree of primary damage is determined at the moment of the receipt of the violence and are a static form of damage. Once done they are done and that is that. They are either fatal or non-fatal; they are sudden and irrevocable.

The secondary pathological occurrences now enter the picture. Unfortunately they may change the picture from a non-fatal to a fatal one. They are not static but are progressive in their development, and are slower in their appearance. Unlike the primary injuries which damage the neurons themselves, they produce their effect by raising the intracranial pressure and embarrassing the cerebral circulation. They can be treated if recognized and a happy outcome will result.

All secondary developments listed above do not occur in every case. Some occur more often than do others. Some degree of shock is usual in every case of severe concussion. Absence of sub-arachnoid bleeding in these cases is rare. Hydrocephalus is usually associated with surface haemorrhages. The only complication of contusion may
be oedema. This oedema may be localized or generalized. The various types of increased intracranial pressure may give rise to signs of hemiplegia, or signs due to herniation or embarrassment of the cerebral circulation.

Patients moribund from the start who show no signs of mental or physical improvement in spite of the treatment usually have received a primary type of injury to the brain which is essentially fatal. Such cases usually die within 12 hours. Here nothing surgical can be done. Death may occur within 12 hours from secondary developments alone, and particularly from the compressive surface haemorrhages. Could these cases be diagnosed accurately early enough, theoretically they could be saved.

When a patient survives for 12 hours or more, very probably he has not received a primary injury of the brain which is essentially fatal and would not succumb if complications did not intervene. Here the role of the surgeon and the therapist is vital and life-saving.

After 24 hours pneumonia and meningitis claim a large death role, and serious injuries in other parts of the body which remain clinically silent are often contributory to death.

IV. DIAGNOSIS

Let us now turn to the problems of diagnosis of the state of the patient suffering from acute cerebral trauma.

Diagnosis in acute cerebral trauma of the closed type is no easy matter. We are presented for examination a patient who is unconscious and often very restless. But our examination, no matter how restless the patient is, must not be postponed. This is an emergency matter.

How often the scene is witnessed where a doctor stands by a bed gazing on a patient, whose spirit is pleading for help, and says, “Well, we’ll let him lie here for a while and see what develops. I think we’ve made him as comfortable as possible. Oh!, by the way, nurse, better take his blood pressure every now and then. Call me if anything develops.” Oh! what a blessing is unconsciousness—for an attitude such as this is a worse fate than being buried alive.

Primary shock must always be cared for before a detailed examination is made. Examination may be deferred for one-half hour, so that the patient may be warmed up. Examination must be carried out in a warm room and under a good light. The patient should be examined with all the bed coverings removed and the patient stripped of all his clothing. First, spend a few minutes in inspection. Analyse the posture of the patient and observe his spontaneous movements. Note his color and the type of breathing.
This done, our examination resolves itself into three distinct phases:

(1) Search for associated injuries.

(2) Signs referable to injuries of the skull.

(3) Signs referable to injuries of the brain.

(1) Search for associated injuries: Too often our whole attention is centred on the head, the obvious cause of the state of unconsciousness. This is an understandable but treacherous fault. For at the same time in other parts of the body associated injuries may exist which are as serious as the cerebral injury, and if left unrecognized and untreated often are the actual cause of death. Fractures of the limbs should be sought for. But more serious than this are the injuries to the chest, the abdomen or the spine. Therefore the abdomen should be palpated for rigidity and percussed for the presence of free fluid or air in the peritoneal cavity; the latter being indicated by a loss of liver dullness. The chest wall should be palpated for fractured ribs and the chest cavity percussed and auscultated for pneumothorax or haemothorax. Also, a finger should be run along the spine to detect possible irregularities from a fracture-dislocation.

On turning to the head itself, it should at first be cleaned up so that it can be seen well. Hair matted with blood must be washed. Wounds of the scalp not accompanied by fracture must be cleaned and sutured. Pools of blood must be dabbed from the ears; otherwise it is impossible to know whether the bleeding comes from a fracture or has merely trickled there from a wound of the soft tissues.

(2) Signs referable to injuries of the skull: In recent years it has been stressed that it is the damage to the brain and its coverings which counts and not the damage to the skull. The pendulum has swung too far from the old teaching of centring the attention on the skull injury. The fracture should be sought for. It points to a force sufficiently great to do great damage to the brain and even though the patient is conscious we will keep him under observation for a while for possible complications. Fracture lines crossing the middle meningeal artery point to the possibility of extra-dural haematoma. Fracture lines are possible doorways for the entrance of bacteria.

Clinical Signs of a Fractured Skull: What do we look for when thinking of the possibility of a fractured skull? One thing we never do is try to elicit crepitus. We may be able to palpate large depressed fractures but not linear fractures. Profuse and persistent bleeding from nose or ears suggests fracture, but the only uncontestable evidence that the skull has been broken is the presence of C.S.F. or brain
tissue in the discharge. Massive sub-conjunctival haemorrhage suggests fracture. As in all fractures the final court of appeal is the X-ray. An antero-posterior and left and right lateral views should be taken.

(3) Signs referable to cerebral trauma: These are the most important and the most complex signs to elicit.

1. All will agree that the outstanding sign of cerebral injury is confusion and unconsciousness. Unconsciousness is a state of extreme gravity and as long as it exists the patient's life is in danger. When it comes on immediately after the injury it is due to diffuse neuronal injury (concussion) or is due to damage of the ganglia of the brain stem or to the thalamus or hypothalamus. It may be perpetuated by secondary compression as the result of the primary injury wears off. A period of consciousness immediately following the accident, however short, as a rule means that any later ensuing state of unconsciousness is due to secondary developments such as an increasing haemorrhage which may be cured by surgical means. The slightest change in the depth of unconsciousness one way or the other is an infallible sign of improvement or regression. As recovery of consciousness is a gradual progress repeated examinations at frequent intervals is necessary if changes are to be recognized early.

Depth of unconsciousness may be judged by reactions of the patient to external stimuli and may be classified thus:

Coma: This is a state of complete unconsciousness in which there are no psychologically understandable responses either to external stimuli or to inner needs. Certain primitive responses such as the corneal, swallowing and tendon reflexes may or may not be present. When absent the state is very serious. The patient cannot be roused or compelled to make a movement by any kind of verbal command or by the infliction of pain such as a pin prick. There is retention of urine, possibly with overflow.

Semi-coma: This is a state of unconsciousness which is not so complete. There is, however, complete lack of co-operation on the part of the patient. The patient will make a movement or change his facial expression in response to painful stimuli. Primitive reflexes are present. In semi-coma the bladder empties reflexly.

Confusion: This is a state of clouding of the consciousness. Here the patient makes an obvious effort to think, but is unable to do so with clarity and speed.

2. Posture and Movements: The study of posture and movements is important as it shows damage to various areas of the brain. We have no time to review the investigation of the nervous system. Suffice to say that there are various levels of function—the basic, reflex move-
ments being located in the spinal cord; the higher control and integration of these lying in cerebral centres and various levels lying between these two extremes. An injury at some particular level, if severe enough, releases the lower centre from the control above the point of injury. These events give rise to various postures and movements which are revealing to the trained eye.

After a severe head injury the patient may lie on his back with his jaw dropped and with his flaccid limbs taking up positions determined by gravity. On the other hand he may be curled up on his side and resist interference. Between these two pictures any kind of position and any kind of movement may be seen. Complete flaccidity of limbs and open jaw means that the whole CNS is in a state of severe shock and if improvement does not appear soon the patient will die. A patient who has only been slightly dazed will look as if he is ordinarily asleep. Prognosis is usually favourable when a patient is curled up on his side and resents being moved from his position.

Of all the other postures I will mention only one: decerebrate rigidity. In this state the patient lies still and the muscle rigidity is persistent, with the limbs usually in hyperextension. When this state occurs immediately after an injury it means that the upper part of the brain stem has been contused, but when it develops after an interval it is due to tentorial herniation, the result of some secondary development such as cerebral oedema or a massive haemorrhage. It demands immediate surgical relief if the patient is to survive.

Restlessness is one of the most common features of any injury to the brain. In many cases a patient lurches from one side of the bed to the other as if seeking a more comfortable position, or he pushes and pulls at the bed clothes incessantly. Often he attempts to get out of bed in a meaningless kind of way. What the significance of all this activity is, is difficult to know. Probably it is a reaction of the patient to the meningeal pain as a result of bleeding into the sub-arachnoid space.

3. Position and movements of the eyes: In concussion a patient’s eyes are usually closed. When they are not it is a sign of approaching consciousness or coma. To differentiate is easy. In coma the corneal reflex is absent or sluggish. In the nearly conscious patient it is very active. One should always observe the eyes to note their position and movements. Various abnormal positions of the eyes are caused by injury to either the third, fourth or sixth cranial nerves. Nystagmus should be looked for.

4. Pupils: The pupils may be contracted or dilated. Often they are unequal and rapid alteration in their size is common—all of which means injury to the brain stem. Of interest and importance is the
“fixed dilated pupil”. Here the pupil is fully dilated and does not react to light shone into it or the other eye. This is a sign of raised intracranial pressure and means that a tentorial pressure cone has developed.

5. Pulse and Blood Pressure: In early stages, when the patient is first seen, the pulse may be fast and thready and the blood pressure low due to the primary shock. This usually returns to normal with warmth and rest. When these signs persist in spite of treatment the prognosis is bad. In the unconscious patient as the condition becomes worse the pulse rises and the blood pressure falls. Where we have raised intra-cranial pressure causing medullary compression we find a rise in the systolic pressure but a low diastolic pressure. Accompanying this we have a slow pulse (60-50 per min.), with a pounding quality.

6. Temperature: The temperature may be subnormal on admission, due to a state of primary shock. Later when heat is applied the body temperature rises, and in coma a patient can readily be over-heated if the temperature of the bed or room is not carefully regulated. In semi-coma a rise of temperature of 1-2° F. is common and is due to absorption of extravasated blood. Fluctuations of temperature within these limits in the first few days is usual and is of no significance. A secondary rise after the temperature has been stabilized for a day or more is often a very serious sign, as it may indicate renewed sub-arachnoid bleeding or the development of pneumonia or meningitis. After severe intrinsic injuries to the brain patients often die in hyperthermia. The temperature rises as soon as shock is passed, and it continues to do so in spite of cold sponging and may reach 111°F. before the patient dies. Any rise in temperature above 101°F., whatever the depth of unconsciousness, is a very grave sign as it is so often indicative of a severe intrinsic injury to the brain or of profuse sub-arachnoid haemorrhage.

7. Respiration: Normal respiration is a good prognostic sign; stertorous breathing is a sign of impending death. Any deviation from the normal rhythm indicates failure of medullary circulation and the patient will almost certainly die if the nature of the lesion is such that it cannot be relieved surgically.

8. Lumbar puncture: This shows the intra-cranial pressure and the presence or absence of blood in the C.S.F. Any value above 150 mm. of C.S.F. indicates an elevation of intra-cranial pressure, assuming that there is no blockage in the cerebro-spinal canal. The elevated pressure may be due to extravasated blood, increased volume of blood within the cranial vessels, oedema or hydrocephalus.

9. Other diagnostic aids such as ventriculography and encephalograms may be employed but are of less general importance.
Let us now apply these diagnostic aids. Using unconsciousness as our criterion we can divide all cases of head injuries into two groups (after excluding those cases which die within a few moments after the accident).

The two groups are:

Group I: Those patients who remain unconscious for an hour or more after the accident.

Group II: Those patients who are only dazed or who recover consciousness shortly after the accident.

Group I: The patient is immediately rendered unconscious and remains unconscious or semi-conscious for a period of hours or possibly for a period of weeks. In civil life the most common cause is an injury caused by the back of the head striking the cement pavement. The fracture, if any is produced, is usually a linear fracture which extends into the base of the skull. Frequently there is no fracture. These patients are seriously ill and may be sub-divided into two groups:

(1)—Patients who appear moribund when first seen and who usually die within 24 hours. These cases are hopeless.

(2)—Patients in who the prognosis is uncertain. There is some hope here.

It is on the basis of the temperature, respiration, pulse, blood pressure and lumbar puncture that we can classify and follow these patients. A chart of half-hourly readings of temperature and blood pressure is of great value. As hours go by information can be accumulated which enables one to give a good or a bad prognosis and occasionally institute some necessary and specific surgical measures.

In sub-group (1) the clinical picture is characteristic. It is not the unconsciousness but the disturbed respiratory rhythm which makes one feel that death is imminent. The respiration is rapid and laboured with accessory respiratory muscles of the neck working. Along with this sign there is complete unconsciousness, a fast, rising pulse, a low, falling blood pressure and a rising temperature. Here the outcome is inevitable and irrevocable.

Sub-group (2) differs from sub-group (1) in that the respiratory rhythm is not seriously disturbed. Profound unconsciousness persisting for more than one-half hour indicates severe brain damage. A fast pulse and a low blood pressure are grave prognostic signs especially if they do not improve in an hour or two. The case becomes hopeless when a rising temperature and a disturbed respiratory rhythm are superadded. A steady pulse and blood pressure, smother respirations and above all a lessening of unconsciousness are all encouraging signs.
In Group I as a whole specific surgical treatment is rarely indicated. Extra-dural haemorrhage is unusual. Although other space-taking lesions such as sub-dural haematoma, sub-dural C.S.F. and localizing intra-cerebral haemorrhage do occur, they are usually the accompaniment of such severe general cerebral injury that no treatment is indicated for them.

In Group II, on the contrary, the diagnosis and treatment of the lesions is of the greatest importance as there is usually a period when successful operation can be done. Simple and compound depressed fractures are more commonly seen in Group II. When the skull gives way beneath a blow the injury to the brain is most marked beneath the fracture and there is no widespread injury and contracoup lacerations which cause prolonged loss of consciousness in Group I.

In diagnosis then:
(1) Make adequate records.
(2) Look for associated injuries of the body which may themselves prove fatal.
(3) Look for fractures of the skull.
(4) Look for evidence of cerebral damage; estimate its severity, and be able to offer a prognosis.

Above all, observe the patient carefully and frequently so changes may be noted. Be able to recognize the rare though typical syndromes of sub-dural and extra-dural haemorrhage and cerebral herniation.

V. TREATMENT

Again let me remind you that we are discussing "closed head injuries". Therefore the principles of caring for the lacerated scalp, the compound depressed fracture of the skull, etc., will form no part of our discussion. We may divide our discussion into two phases:

I. Those aspects of treatment which are non-controversial.
   (a) First Aid.
   (b) Nursing Care.

II. Those aspects of treatment which are controversial.
   (a) Use of therapeutic drainage of cerebrospinal fluid.
   (b) Use of intra-venous dehydrating agents.

As a preface to the remarks that follow it can be said that, inflexible, routine treatment of patients suffering from head trauma is not only useless but dangerous; no other group of surgical patients demands such individual attention and consideration. Excellent therapy for one patient may be poison for another; yet the two patients, to superficial examination, are not unlike in their clinical manifestations. Alert, watchful care is perhaps the most important feature. Since the
patient’s condition may vary from hour to hour, continuous efficient
nursing care is of prime importance.

(a) First Aid: In regard to transportation of the patient by
ambulance to a hospital it may be said that closed head injuries travel
well in a modern ambulance and may be sent long distances for
treatment. If distance, therefore, is the only consideration, it is much
wiser to transport a patient directly to a hospital which is specially
equipped for treatment of cerebral trauma than to an institution which
is not fully prepared for the work. During transportation a free airway
must be maintained to prevent congestion, and for this reason the com­
tose patient should be turned on one side and not allowed to lie on his
back, in order to prevent the tongue from falling backwards and
impede respiration. This position also allows saliva to trickle outwards
which otherwise might be aspirated into the lungs.

The importance of a free airway at all times in the deeply uncon­
scious patient cannot be overstressed. McKenzie on the matter says:
"The maintenance of a free airway is considered to be of the utmost
importance. Any obstruction to respiration such as the tongue
dropping back, prevents expansion of the chest and dams venous blood
back into the brain. Thus further haemorrhage may be produced. In
general it may be stated that the maintenance of a free airway is more
important than any other therapeutic measure in the deeply comatose
patient. The tongue and jaw must be kept forwards. Usually this
is simply accomplished by having the patient placed on his side. A flat
airway such as that used in anaesthesia is of value. Occasionally a
special nurse may have to hold the jaw forward."

Unless absolutely necessary drugs such as morphine should be
avoided. The administration of these drugs, especially at an early
stage, may mask important neurological signs.

(b) Nursing: The nursing of the patient is very important. Except
in a neurological institute the nurse will have to be specially instructed.
First of all, the nurse must make recordings of the temperature,
respiration and the pulse, the amount of fluids taken, blood pressure
readings and changes in depths of unconsciousness. Records are kept
in the form of a graph on the same chart. They should be made at
intervals of one-half hour for the first 24 hours at least. After im­
provement of the patient, hourly records are sufficient. These are the
minimum requirements. By this means only a continuous clinical
picture of the patient can be obtained, and this is necessary if the
patient is to receive the best possible treatment.

Now I wish to discuss some specific and important points in the
nursing procedure.
1. Restlessness:

The patient with a head injury is very often restless and uncooperative. The patience of the nurse and attendants is taxed to the limit if they have had no neurological training. It is the greatest temptation to use violence with the patient and handle him like an animal; to tie him in bed. These things are wrong. The restlessness is due to irritation of the meninges by blood. It is in nature much like a form of meningitis. The patient then should be handled like a patient with meningitis, gently, and refraining from making any forcible movements of the limbs or neck which merely cause further pain. In the restless state the mind is open to suggestion and a kind or encouraging word to the patient is never wasted though it often seems to be. By raising and padding the bed sides and by having someone constantly in attendance to prevent the patient from getting out of bed, he may be allowed considerable freedom.

As stated above, drugs should be avoided if at all possible. But the patient may become so restless that he is harming his own condition; in these cases a barbiturate or paraldehyde may be given. You must give the drug in the minimal amount to give the desired effect. To give more is dangerous. To give less is useless.

2. Feeding:

Patients are usually able and willing to swallow. When they cannot do so they must be fed by a stomach tube. No fixed rules for feeding can be given. Glucose in water is the only drink which needs to be given in the first 24 hours. The minimum is 1 oz. per hour for the first 24 hours. On the second day larger quantities of fluid may be given according to the state of the patient. Here, give a minimum of 2 pts. and a maximum of 3 pts. Milk drinks may be given alternatively with water. On the third day it is essential to introduce some kind of protein-containing food, otherwise the patient will live on his own tissues and die from exhaustion. Junket, egg and custard are of value.

3. Bowels:

There is serious risk of incontinence when aperients are given to an unconscious or semi-conscious patient. This, associated with the restlessness, would obviously be a very distressing situation. Should it occur it should be controlled with bismuth and opium. Magnesium sulphate by mouth is often advocated in amounts large enough to produce a watery stool. As an alternative the bowel may be emptied by an enema. Cathartics such as calomel should never be given.

4. Bladder:

Incontinence is not uncommon and necessitates constant changing of the bed linen if the patient is not to become uncomfortable or his
skin broken. On the other hand, retention may exist. Here, catheritization is necessary; otherwise the discomfort of a distended bladder will make the patient restless or compel him to try to get out of bed to relieve himself. As consciousness approaches the patient should be encouraged to try to use the bed pan or urinal according to the sex.

5. The Skin and Mouth:
These need caring for to keep them clean and in good condition.

6. Temperature:
The initial shock should be treated with heat. A rise in temperature of 2° F. or more should be treated by tepid sponging.

Now we must come to grips with the more controversial aspects of treatment. What are we going to do for the raised intra-cranial pressure? Is elevated intra-cranial pressure very common in closed head injuries? About these points of discussion great scientific battles have raged. Some have maintained that vigorous means should be employed to combat the raised intra-cranial pressure resulting from cerebral oedema such as the use of dehydrating hypertonic solutions intravenously and drainage of sizeable amounts of C.S.F.

About these controversial matters let us state the case simply:

(1) Increased intra-cranial pressure is not the major problem in many cases of severe head injury.

(2) The routine use of hypertonic solutions, for purposes of dehydration, is a practice which cannot be condemned too severely. This form of would-be treatment has gained alarming popularity. There is no justification for the routine use of dehydrating agents in treatment of head injuries.

(3) As a therapeutic measure, spinal puncture is of little or no value and may be harmful in acute head trauma—possibly resulting in immediate death—if done in the presence of greatly elevated intra-cranial pressure. There comes a time, however, in many cases of head trauma, when therapeutic lumbar punctures are exceedingly valuable. Blood in the C.S.F. is an irritant, and after haemorrhage has ceased and the contaminated blood is being absorbed, irritative meningitis is a serious problem. Spinal drainage at this stage of meningeal irritation relieves symptoms dramatically. The procedure should be repeated once or twice daily until the fluid is almost free of color. There is considerable evidence to indicate that the late drainage of blood-contaminated C.S.F. may be of value in preventing post-traumatic sequelae.
VI. Conclusion

The importance of injuries to the head increases each day. In every speeding automobile is a potential head injury. Of the eight to nine thousand deaths on British roads each year, 80% are due to head injuries. For every person who dies as a result of a head injury, four others receive non-fatal injuries to the head which lead to prolonged morbidity. Such complications as post-traumatic headaches, post-traumatic neuroses, post-traumatic epilepsy and post-traumatic deafness will then be common.

Prevention, I am afraid, will play little part in this field of medicine. Reduction of mortality will depend on more accurate diagnosis and improved treatment. The horizon is far from cloudy in this respect. Amazing reduction in mortality rates in head injuries were achieved in World War II as compared with World War I. With such an improvement as a stimulus there can only be a bright future for the patient dulled by a blow to the head.

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Allergy: A Review of Its Mechanism and Management

By F. P. Scarfone, Meds '48

Allergy represents a symptom complex of varying characteristics depending on the chief organs involved. References to the condition can be found in early Greek and Roman writing; Pliny describes the condition in the Chinese literature of his day; and legend indicates the condition was known to the North American Indians.¹

Early in the twentieth century rapid strides began to be made in the field of allergy. In 1902 the term anaphylaxis was coined and appeared in the literature. Anaphylaxis is defined as the "term applied to the symptoms which arise from a violent union of antigen with antibody in the tissues." In 1906, von Pirquet introduced the term allergy. Allergy can be defined as a "changed reaction capacity which the human or animal organism gains through recovery from disease or through treatment with foreign substances."¹⁷ Koch was the first to record the allergic reaction, and it has since been termed the Koch phenomenon. In the course of his observations on the tubercle bacillus he found that a second intraperitoneal injection of tubercle bacilli into a guinea pig resulted in the appearance of an inflammatory reaction surrounding the site of the first needle puncture.¹⁸

These early workers carried their knowledge of immunology into the study of allergy and anaphylactic shock.

A review of some of the basic immunological considerations will aid in the understanding of allergy.¹⁶ "Antigens"—are any substances which can give rise to the development of specific antibodies in the circulation of animals to which they have been administered in such a manner as to avoid a change in structure. Such a substance must be protein in nature. Specificity is inherent—i.e. antibodies are produced which react subsequently only with the inciting antigen, or other antigens that are closely related in chemical structure. "Haptenes (Partial Antigens)"—before these substances can act as an antigen they must be combined with a protein. The haptene portion of the antigen. Haptenes may be simple chemical compounds such as acetyl antigen. Haptenes may be simple chemical compounds such as acetyl salicylic acid.¹⁴

"Antibodies"—are serum globulins which differ from the normal globulin of the same animal largely in being of greater molecular size. These globulins are produced by the body in a response to the presence of a foreign protein (antigen) in the body.
Ehrlich theorizes that antigen and antibody react in the following fashion: Antigen and Antibody enter into a chemical union; each antigen possessing a specific atom group by means of which it is bound to a pre-existing side chain of the affected cell, much as the Hydrogen ion combines with the chlorine ion to form hydrochloric acid. 16

All forms of hypersensitiveness are divided into two classes. A. hypersensitiveness in which an antibody mechanism has been plainly demonstrated; B. hypersensitiveness which, while retaining a specifically increased reaction capacity for an antigenic substance or for partial antigens, occurs without definite evidence of the presence of circulating antibodies.

Desensitization: requires a gradual introduction of the antigen in such a manner that the union with the sessile antibodies may be a slow one (i.e. with those located in the tissues) leading to a gradual saturation, and avoiding the sudden acute change which would follow upon more violent reactions. This can be accomplished either by a very slow injection of diluted antigen or by repeated injections of small amounts.18,18,4

Duration of Sensitiveness and Desensitization: Once the cells of an animal have come into contact with an antigenic substance they are never again normal in relation to this substance. Long after active antibody production has ceased, the cells are still in a condition in which contact with this antigen will stimulate them to an antibody production more energetic than normal. Sensitiveness will probably last to some degree throughout life. Desensitization lasting only as long as the cell antibodies remain reasonably saturated.16 This suggests two methods of preventing anaphylactic symptoms in sensitized individuals: 21. 18
1. Permanent removal from possibilities of contact with the antigen.
2. Constant and repeated desensitization.

The production of allergy and allergic reaction in man can be outlined as follows: 21

1. The individual is sensitized to an antigen e.g. pollen.
2. The sensitized individual produces specific antibodies to the antigen and fixed antibodies settle in the tissues of the body. The tissues of maximal concentration of fixed antibodies are called “shock organs” and determine the localization of clinical manifestations.
3. On renewed exposure to the antigen an antigen-antibody reaction occurs which is maximal in the “shock organ”.
4. The reaction leads to a release of Histamine or Histamine-like substance. The source of this histamine are the tissues of the sensitized individual. It is released into the blood and lymph.
ALLERGY: A REVIEW OF ITS MECHANISM AND MANAGEMENT

Histamine is a normal constituent of many tissues. It is not uniform in its distribution throughout the varied tissues of a given animal species nor uniform for a given tissue in various species.\(^5\)

It is evident that the nature of the anaphylactic reaction depends on the site of the shock organ. The fundamental physiological activities of histamine are:\(^6\)

1. Spasmogenic action on smooth muscles of bronchioles, uterus, ureter, gall bladder, and gastro-intestinal tract.
2. Dilatation and increased permeability of capillaries, which is important in the production of edema.
3. Increased secretion of various glands—lacrimal, salivary, gastric and pancreatic.

The cellular discharge of histamine is not the result of a destruction of the cells involved, but probably a specific change in permeability of the cell wall permitting the escape of histamine.\(^8\)

Human hypersensitiveness or the production of an allergic response is invariable and can be expressed in chart form.\(^1\)


Principal clinical expression of the disorder:

1. Bronchial asthma, hay fever, vasomotor rhinitis, gastrointestinal disturbances, acute urticaria, and other skin lesions.
2. Bronchial asthma, vasomotor rhinitis, chronic urticaria.
3. Eczematous skin lesions.
4. Skin eruptions, fever, visceral lesions.
5. Fever, arthralgia, urticaria.
7. Periarteritis nodosa.

Atopy:—An hereditary disorder involving specific antigen-antibody combination which results in release of histamine or histamine-like substance producing edema, smooth muscle spasm and increased secretion of mucus in the selective tissues involved. These tissues or "shock organs" are chiefly respiratory, gastro-intestinal, mucous membranes and the skin.

Atopic-like disorders:—The symptoms and lesions are identical with those of atopy, but no immunological response can be demonstrated. In this group of individuals there is no hereditary history, no skin reaction and no therapeutic response from the protective measures against...
common allergies. This group includes asthmatics. It may be due to histamine release apart from an antigen-antibody reaction.

*Contact dermatitis:*—No antibodies have been demonstrated in this process. Materials responsible for this are not antigens—e.g. mercuric chloride, formaldehyde, starch. It is possible, however, that they may act as haptenes and form antigens. The fact that it is an expression of hypersensitivity is shown by the necessity for repeated exposures to occur before symptoms develop.

*Drug Allergy:*—It is due to linkage with body protein to form antigens which in turn stimulate antibody formation.4

With the basic mechanism behind allergy as a background we will now consider some aspects in the management of the allergic reactions. Detailed descriptions will only be given for the newer antihistamine drugs.

Desensitization is an important procedure in the management of the allergic patient. This is, however, a difficult, tedious and not always safe task. The antigens responsible are numerous; amongst them are pollens, foods, animal epithelium and air-borne fungus spores.18 Rational therapy requires a determination of the specific antigen or, more usually, antigens. This is accomplished by using prepared portions of antigen in the scratch test, intracutaneous tests and opthalmic tests. Once the offending antigen has been determined specific desensitization can be started. Basically, this involves the repeated injection of sublethal doses of specific antigen. This is a slow, tedious process requiring numerous injections, achieving moderate although usually clinically adequate tolerance and demonstrating a great tendency for rapid loss of tolerance when injections are discontinued.

The establishment of histamine as a factor in the allergic response led to two methods of non-specific desensitization.

1. Histamine—Azoprotein (Hapamine), a protein conjugate of histamine is used as an antigen in an attempt to produce antibodies to histamine. If successful, histamine liberated by the allergic response would be neutralized by the antibodies thus preventing the development of allergic symptoms. Clinically some good results have been claimed, but critical studies show hapamine has little use in the management of the allergic patient.18, 6

2. Histamine Desensitization—In this method it is anticipated that repeated injections of gradually increasing amounts of histamine will render the “shock organs” less susceptible to histamine liberated with the union of antigen-antibody. Clinically it has been of limited value in the treatment of histamine cephalgia, and primary vaso-dilative type
of migraine. Urticaria has shown some response, but it has been disappoint ing in other allergic disorders.\(^8\), \(^18\)

The newest trend in management of the hypersensitive response in man has been the use of histamine antagonistic drugs. These drugs are all similar in possessing certain phenolic ethers.

The starting point for the development of the subject of modern anti-histaminic drugs was in 1933. At this time Fourneau and Bave t demonstrated that certain phenolic ethers possessed anti-histaminic powers both in vitro and in vivo. Many similar compounds were studied in French laboratories. Recently the French introduced two new anti-histaminic drugs—antergan and neoantergan. In the last few years American pharmaceutical laboratories have developed a number of anti-histaminic drugs. Three of these drugs now used extensively are Benadryl, Pyribenzamine and Antistine.

Before any drug is used therapeutically a knowledge of its pharmacology is necessary. For this reason, a brief outline of their pharmacological action will be given.\(^10\)

Therapeutic doses of these anti-histamine drugs are able to antagonize the liberated histamine without eliciting a pharmacological response, or if a response is produced, it does not appear to be of a type or degree to suggest an important causal relation to histamine antagonism.

Large doses may produce one or a number of the following side effects: 1. Marked respiratory depression. 2. Marked excitability. 3. Tremors. 4. Convulsions. 5. Secondary respiratory depression at times.

Effects are seen on various systems of the body:

(a) Local—This group of drugs exerts some local anaesthetic effect. This action may be of value in vascular and cutaneous responses in which axon and other reflexes are involved. This will thus explain the antipruritic effect and the production of cutaneous analgesia.

(b) Cardiovascular—Rapid intravenous injection in dogs produces a transient hypotension. This is accomplished by the production of a vasoconstriction of the blood vessels in the intestines, spleen and kidney; and a vasodilatation of the vessels of the extremities. Therapeutic oral dosage over a period of several weeks seldom lowers the systolic blood pressure. No clinically detectable variations in the cardiac rhythm or rate have been demonstrated.

(c) Central Nervous System—Toxic doses of all anti-histamine drugs stimulates the central nervous system of animals bringing about hyperexcitability, tremors and convulsions.

In man sedation is produced. This sedation varies in degree from
person to person. Such a side effect has frequently been encountered with benadryl, less frequently with pyribenzamine and has been known to occur following the use of antergan and neoantergan.

(d) **Gastro-Intestinal Tract**—Gastric distress, nausea, emesis, colic and diarrhea occur. They are seldom seen with benadryl but occur more frequently with antergan, neoantergan and pyribenzamine. An explanation for this difference may be that they are practically devoid of anti-spasmodic properties but are capable of inducing spasm of intestinal and uterine muscles of animals in vitro and in vivo.

The absorption, distribution and excretion of the phenolic ether group of drugs: they are rapidly absorbed and gain an early generalized distribution. Nothing is known of their destruction, conjugation, deposition or excretion.

Antagonism of histamine by these drugs is known to occur in various systems of the body. Examples of this can be seen in the following:

(a) **Bronchioles**—This group of drugs is highly effective in antagonizing bronchoconstriction, in intact guinea pigs, brought on by exposure to a histamine aerosol or to intravenous injection of histamine.

(b) **Intestinal Musculature**—The majority of anti-histamine drugs do not prevent spasm or exert prominent relaxing effect on intestinal muscles except under conditions where histamine has produced increased tonus, hypermotility or spasm.

(c) **Uterine Muscle**—Anti-histamine agents, with the exception of benadryl, are capable of contracting uterine muscle; all antagonize the spasmogonic action of histamine on the uterus.

(d) **Capillary Permeability and Cutaneous Reactions**—Histamine is a very potent substance in increasing capillary permeability. Large amounts of histamine are present in the skin. It has been demonstrated that diminishing capillary permeability is solely an anti-histamine action. These drugs—possessing a local anaesthetic effect—prevent histamine from initiating the axon reflex which is partly responsible for wheal formation.

(e) **Glandular Secretion**—It has been shown that histamine-induced lacrimation is definitely suppressed after administration of anti-histamine drugs.

Can these drugs be used in effectively treating severe forms of anaphylaxis? Experimentally it has been shown that anaphylaxis has been alleviated in intact guinea pigs by administration of antergan, neoantergan, pyribenzamine and antistine. In untreated sensitized dogs a 34.6% mortality was reported following injection of horse serum.
contrast to this 22 dogs were treated with benadryl during administration of the horse serum. This group showed no fatalities.\textsuperscript{10}

In summary, the pharmacological action of this group of drugs it can be stated that antergan, neoantergan, pyribenzamine and antistine exert a low and probably insignificant degree of atropine-like action. These drugs can be regarded as a fairly specific group of antagonists of histamine.

There are three possible ways in which the drugs may act in inhibiting the action of histamine; but the exact mechanism is unknown.

(1) An indirect physiological mechanism—e.g.—epinephrine induces a biological response which is diametrically opposite and independent of the action of histamine in producing bronchospasm, vasodilatation, increased capillary permeability and contraction of intestinal muscles. It is apparently non-specific in character.

(2) Rendering the drug inactive as by reduction, oxidation, conjugation or formation of salts or complexes.

(3) Direct antagonism may involve competition between two substances for a given site of action. This type of antagonism is reversible and one of the most specific in nature.

Experimental and therapeutic evidence indicates that the major action of anti-histamine drugs is probably exerted directly on peripheral effector cells which respond to histamine since antagonism has frequently been demonstrated in isolated tissues or organs. The antagonism exerted peripherally could be modified by nervous or humoral influences in the intact animal. This action is analogous to the displacement of p-amino-benzoic acid by the sulfonamides.

Therapeutic use of anti-histamine compounds is not free from side effects.\textsuperscript{9} The reactions that occur most frequently are: drowsiness, weakness, stupor, narcolepsy, confusion, somnambulism, dizziness, indigestion, numbness, cold extremities, jitters, collapse, exhaustion, palpitation, irritability, aggravation of allergic symptoms, hot flashes, pallor, nausea, bad taste, dry mouth, sore tongue and blurred vision. When these symptoms occur they are severe enough in a portion of the cases to warrant stopping the drug being used. In some patients reduced dosage, despite mild symptoms, will overcome the tendency to such reaction. Subsequently larger doses, with better therapeutic results, will usually be tolerated. Frequently the symptoms will disappear within 24-48 hours, even though the patient continues to take his medication. With this general outline in the background, the use of anti-histamine compounds in the scientific therapy of hypersensitive states in man can be discussed. Remarks will be limited to benadryl,
pyribenzamine and antistine which are most commonly used on the North American continent.

Anti-histamine drugs can be used effectively in the treatment of the following conditions:5,21

1. Urticaria. 2. Angioneurotic edema. 3. Hay fever. 4. Vasomotor rhinitis. 5. Serum sickness. They are moderately effective in asthma.

The following conditions are well controlled:

1. Pruritus of atopic dermatitis.
2. Pruritus of other dermatoses including pruritus vulvae.

An outline for the administration of this group of drugs will be given:19

For adult patients the initial dosage is 150 mgms. daily. This is increased by 50 mgms. per day until a maximum of 600 mgms. daily is administered, or until symptoms are relieved. Occurrence of undesirable side effects may require stoppage or a decrease in dosage of the drug. The effective dosage of the drug is then continued for a minimum period of two weeks. At the end of this time the drug is discontinued. With recurrence of symptoms the patient resumes treatment with 150 mgms. or less per day. If relief does not ensue in one or two days, the last effective dose of the drug is again taken.

In children the dosage is calculated at 2 mgms. per pound of body weight. The initial daily dosage is 60 mgms. daily and is increased 10-20 mgms. per day until the maximum or optimal dosage is administered. The elixir preparations are more convenient for therapy in children. These elixirs contain 10 mgms. to each teaspoonful dose.

Observations made in the treatment of a large number of cases of allergic hypersensitiveness in man can be applied to the basic principles in anti-histamine drug therapy of the allergic states. Some of the more important will be enumerated below:

1. Daily dose in adults varies from 50-600 mgms.19
2. Infants and children are best treated with an elixir form of the drug. The average daily dose that is required being 20-100 mgms.11
3. In acute cases the response is prompt.7
4. If no effect is noted within two hours the dosage may be inadequate.7
5. If a trial of increased dosage over a period of twelve to twenty-four hours does not show a reasonably satisfactory control of symptoms, the treatment must be considered unsuitable.7
6. In milder and chronic conditions a low daily dosage and a longer trial period may be necessary.  
7. The mild sedative effects, if undesired, can be combatted with small doses of caffeine, ephedrine or benzedrine.  
8. Gastric discomfort can be reduced to a minimum by taking the drug immediately following a meal, or preceding the drug by a glass of milk and a biscuit.  
9. As the anti-histamine drugs are not synergistic with the sympatho-mimetic group of drugs, they can be used together. They may also be combined with other drugs such as aminophyllyne. In hay fever, combinations of the anti-histamine drug with ephedrine and aminophyllyne, are more effectual than the use of any one drug alone.  
10. Because of the hypnotic effect of these drugs, care must be used in prescribing barbiturates and other sedatives with them.  
11. Side reactions, if not too severe, are not an indication to deprive the patient of the drug.  
12. If more rapid effect is desired, the drug is given without previous food.  
13. Drug allergies as are seen with penicillin, liver extract, barbiturates, sulfonamides, atabrine, etc., can at times be sufficiently relieved to allow a continued administration of these drugs when continuation is therapeutically indicated.  
15. Loew has shown that adequate doses of benadryl augment the response to sympatho-mimetic drugs.  
16. The earlier in an attack the drug is administered, the more prompt and complete is the relief obtained.  
17. As the benefit obtained from these drugs is symptomatic, and lasts for only a few hours from each dose, it is important that desensitization treatment not be abandoned in favour of this form of therapy.  
18. When side reactions occur before symptomatic relief with benadryl is obtained, pyribenzamine may be substituted. One half patients treated with benadryl have side reactions, while only one quarter of those using pyribenzamine have this difficulty.  
19. There is no significant difference in protective ability on intact animal or isolated sensitized strip of guinea pig between benadryl, pyribenzamine, antergan and neoantergan. The protection, however, decreases as the dose decreases.
Allergic conditions do not respond fully nor to the same degree to treatment with anti-histamine drugs. Various investigators give different figures for relief of symptoms. The following table is given to give a general indication as to what can be expected in therapy.5,15,21

<table>
<thead>
<tr>
<th>Condition</th>
<th>% Benefited</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>12-65%</td>
</tr>
<tr>
<td>Migraine</td>
<td>63%</td>
</tr>
<tr>
<td>Hay Fever</td>
<td>60-75%</td>
</tr>
<tr>
<td>Urticaria—acute</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>chronic</td>
</tr>
<tr>
<td>Allergic Rhinitis—children</td>
<td>66%</td>
</tr>
<tr>
<td></td>
<td>adults</td>
</tr>
<tr>
<td>Atopic Eczema</td>
<td>75%</td>
</tr>
<tr>
<td>Generalized Contact Dermatitis</td>
<td>66%</td>
</tr>
<tr>
<td>Sulfa Drug Eruption</td>
<td>50%</td>
</tr>
</tbody>
</table>

From the above it is apparent that anti-histamine drugs are not a panacea for all diseases associated with allergy. Older methods of elimination and desensitization are not to be discarded in favour of therapy with the newer anti-histamine drugs. They can, however, be combined with them to make the treatment more effective.20

Allergists give the following as indications for management of allergic conditions with the newer anti-histaminic drugs:8

(a) To control diffuse skin irritability and dermatographia to permit the performance of specific skin testing for determination of the offending antigen.
(b) To control and prevent treatment and testing reaction.
(c) To maintain allergy patients in comfort until the specific desensitization becomes effective.
(d) To control acute transient allergic manifestations.
(e) To control pruritus, minimizing scratching and indirectly avoiding infections.
(f) To control urticaria which may have followed sulfonamide, antibiotic, organ extract, serum and other indispensable drug therapy.
(g) To control gastric acidity in a small number of cases.

Allergy is an important disorder that must be coped with in the practice of medicine. Estimates show that two to five per cent of the population suffers to some degree from this affection.18 Any condition occurring so frequently should be understood by the general practitioner. Scientific therapeutics demand individualized treatment as dictated by the principles of pharmacology, physiology, pathogenesis and pathology. For this reason the management of allergic conditions has been discussed subsequent to the basic principles behind allergy and the hypersensitive state.
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HOSPITAL CARE OF THE SURGICAL PATIENT

By

Geo. Crile, Jr., M.D., Surgeon, Cleveland Clinic

and

Franklin J. Shively, Jr., M.D., Asst. Surgeon, Cleveland Clinic


This is a surgeon's handbook which presents "in one small volume the clinical, physiologic and technical principles that have become so important in the hospital care of the surgical patient." It is divided into six sections, including: The Physiological Principles Related to the Care of the Surgical Patient, which is devoted chiefly to a discussion of the mechanism of fluid balance; management of Surgical Complications, detailing twenty-six such conditions often encountered; the procedures required in properly preparing the patient for operations; valuable suggestions and specific measures for post-operative care; technique of Common Hospital Procedures; the relation of the House Officer to patients' relatives, attending surgeons, nurses, and personnel of other departments of the hospital. Each House Officer and young surgeon will find this book a valuable ready reference in solving many of his everyday problems.

—Ronald M. Smith, '49.

A DOCTOR IN THE HOUSE

By Henry Pleasants, Jr., M.D.


Henry Pleasants, Jr., in this small volume, has put the story of his life into a very attractive form. A real insight into the life of a doctor is presented, both as general practitioner and specialist.

Numerous unusual case histories are presented in condensed form to illustrate the main theme of each chapter. These serve to arouse the
BOOK REVIEWS

interest and curiosity of the inexperienced, but to any trained diagnosti­
cian would seem grossly inadequate. Any deficiency in this aspect is
balanced, however, by the human interest and humour present through­
out the pages.

The writer discusses the ever-present problem of fees, specialties, labo­
atory assistance in diagnosis, drawing extensively from his own ex­
perience. The last chapter is devoted entirely to a discussion of the fate of rural general practitioners. Special emphasis is placed upon changes which should be made in training the country doctor of the future.

Although not a classic, this book makes very pleasant and profitable div­
erion from the prescribed medical texts, which take so much of the student's time.

—P. Yates, '50 B.

MY BROTHER JONATHAN

By FRANCIS BRETT YOUNG

WILLIAM HEINEMANN LTD., LONDON, TORONTO, 1928, pp. 331.

PRICE: $2.50. (REPRINT 1947.)

The setting for this novel is England just before the First Great War. The hero is Jonathan Dakers, a sincere, trusting, good-natured chap who, throughout most of his life, plays a very complete “second fiddle” to his brother Harold. Harold reaps all the attention, money and praise that the eccentric Dakers household can muster, while the steady, plodding Jonathan, by true perseverance, works and sweats his way through medical school.

After graduation Jonathan shoulders the burden of maintaining his mother and brother when Eugene Dakers, the father, is suddenly killed and leaves as his estate a few volumes of his own poetry and several debts. Harold is put through medical school at Jonathan’s expense, with the hope that, on receiving his degree, he will work with Jonathan, who has developed a successful practice in the small coal mining town of Wednesford. This hope is dissolved when Harold finds that the village existence does not appeal to him.

Jonathan’s struggles to get himself established and accepted in Wednesford, where he starts as an assistant to Dr. John Hammond, keep the reader thoroughly engrossed. Always in the background is Rachael Hammond, whose quiet support and confidence aids Jonathan to acquaint himself with, learn to understand, and finally to love, the coal mining inhabitants of the district.
I found this book extremely interesting and it enters the category of "once you start it, you can't leave it alone". The characters are real and so excellently portrayed that one has no difficulty in visualizing them. I suggest that anyone with a few hours to spare and searching for a book to read would not feel that he had made a poor selection in "My Brother Jonathan".

—J. C. Parry, Meds '50 B.

INTERNAL MEDICINE IN GENERAL PRACTICE

By Robert Pratt McCombs


A very successful attempt has been made by the author to correlate the diagnostic aspects of medicine—history, physical examination and laboratory procedures—in order to present a complete but concise picture of all the common disorders as well as some rarer forms of disease. An up-to-date section on therapy is included with each topic.

Accompanying the discussion are important pathological facts and an integration of physiological principles with the clinical aspects of internal medicine.

Valuable and sometimes formidable lists of diseases are outlined, in which a common symptom or sign is found. No attempt is made to provide a complete differential diagnosis in this book, which is confined to discussion of basic principles of diagnostic and therapeutic methods.

This book is expressly designed for quick consultation by the busy practitioner and is not intended to be an intensive reference work. Graduating students would also benefit immensely if this book were easily accessible to their searching minds.

To Study the Phenomena of Disease without Books

Is to Sail an Uncharted Sea.

—Oeier.

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January 13, 1948.
CARONAMIDE—INHIBITOR OF PENICILLIN EXTRACTION
Applied to Treatment of Subacute Bacterial Endocarditis

BOYER, ET AL

Preliminary clinical study has shown that the plasma concentration of penicillin is increased three to seven times by the oral administration of caronamide. This substance has caused no serious toxic effects.

It is thought to cause "a physiological and reversible inhibition of penicillin transport, due to a substrate competition between penicillin (excreted by the renal tubules) and 4'-carboxy-phenylmethanesulfonanilide (which is essentially refractory to excretion by the transport mechanism)."

Because of the encouraging results of these studies, caronamide was tried in a difficult case of subacute bacterial endocarditis, caused by a penicillin-resistant strain of streptococcus viridans.

The patient had undergone four courses of antibiotic therapy—two of penicillin and two of streptomycin, but recurrences had followed each course. Sensitivity tests showed that the sensitivity of the organisms had decreased considerably during treatment.

For the fifth course, 4,000,000 units of penicillin were given per day for 28 days. This was supplemented by oral caronamide for 25 of these days, in doses varying from 12 to 24 grams per day.

The effect of these varying doses on the plasma levels of penicillin was determined and the latter were found to be much higher and more prolonged than without caronamide.

Levels of 30 to 60 units of penicillin per c.c. were obtained. Without caronamide these would require at least 10,000,000 units of penicillin per day. The effect, however, is not constant for different patients, or even the same patient on different days.

The authors suggest the measurement of phenolsulphonphthalein excretion as a test for penicillin excretion, since both are eliminated by the renal tubules. This test could regulate the dosage of caronamide.

Toxic effects of caronamide, including a few red blood cells in the urine, suggest transient renal damage, but no serious effects were noted.

—SYDNEY ROSEN, '48.

HEART MURMURS
(Part 1)

By WILLIAM EVANS
Br. Heart J., 9:101; 1947

By the use of a phonocardiogram the author has been able to accurately record heart murmurs sometimes not evoked on clinical auscultation. The phonocardiographic recordings are made synchronously with an electrocardiogram, thus the murmurs are placed in their exact position in the cardiac cycle. In this article he considers the innocent mur-
murs of the mitral area, and the murmurs of mitral valve disease.

Concerning these innocent murmurs the author gives an excellent clinical classification which has been verified in a large series of cases, by the phonocardiogram. The innocent murmurs are classified as follows:

The soft murmur of the reclining posture, the soft murmur of the upright posture, the loud murmur unaffected by posture, and the loud parasternal murmur. The other mitral murmur is loud, unaffected by posture, and heard in systole.

The author has shown that all cases of mitral stenosis have a mid-diastolic murmur, although it sometimes cannot be heard clinically. In further studying the murmurs of mitral stenosis, he found that the presystolic and systolic murmurs began during auricular systole.


INFECTIOUS HEPATITIS

MARTIN RANDOLPH and ALFRED DE VITO

The typical case of infectious hepatitis seen in hospital occurs in the fall and winter months. In this series, it was a child, usually female, of about eight years who came in with an abrupt attack of nausea, vomiting, abdominal pain, and a fever of 100-101°. The pre-icteric period lasted about seven days. One to two days before the end of this period the urine became dark and the stools light.

The icteric stage lasted for about 14 days and showed a gradual subsidence of the pre-icteric symptoms in one to three days. There was no fever at this stage, rarely pruritus, and no bradycardia. In 60% of the cases the liver was enlarged.

The laboratory findings showed: urine positive for bile in the late pre-icteric and icteric stages, stools positive for bile at all times, Van Den Bergh immediate and direct, icteric indices from 24 to 126, and prothrombin 63%.

There was no mortality and the average stay in hospital was nine days.

—R. N. BISSONNETTE, '49.

GASTRIC CARCINOMA

By ABRAMSON and HINTON
S.G. & O., 84:481-89; 1947

The second commonest cause of death in people past 30 years of age is carcinoma. One-fifth of all cases is due to carcinoma of the stomach. Hence the study of gastric carcinoma is of utmost importance and worthy of repeated analysis.

The authors have reported a series of 583 cases of carcinoma of the stomach occurring between 1918 and 1945. Comparative studies of these cases demonstrate poor prognosis and the lack of progress in treatment.

Since there is no relationship between the onset of symptoms and the operability of the cancer, diagnosis of early cases is almost impossible.

Investigation of these cases does not substantiate the possibility of the transformation of benign gastric ulcer to gastric carcinoma, and the author concludes that such transformation occurs only rarely. The following four factors do seem to have a definite relationship: (a) age and sex incidence; (b) chronic gastritis; (c) endocrine effects on the gastric mucosa; (d) the inception of gastric neoplasms.

The authors put forward a plan designed as a means of discovering curable malignant conditions. This plan includes:

1. Education of the public.
2. Fluoroscopic and X-ray studies of the stomach, performed as part of an annual physical examination and as a routine on patients over 40 years of age entering hospital.
3. Availability of fluoroscopic and X-ray examination for every economic level.
THIAMINE AND ARSENICAL TOXICITY

Preliminary Report—G. B. Sexton and C. W. Gowdy
Arch. Dermat. and Syphilology
56:634-647; 1947

The authors point out the similarity between arsenical encephalopathy and Vitamin B1 deficiency, both in their clinical manifestations and biochemical effects.

Five cases of acute arsenical intoxication are described. In all of these there are manifestations of a derangement in carbohydrate metabolism, as shown by increased pyruvic acid and sugar in the blood. The high level of pyruvic acid suggests that catabolism is stopped at the level. A deficiency of the coenzyme containing thiamine produces a similar high level of pyruvic acid.

Experimentally, a sudden rise in the level of pyruvic acid, with greatly increased muscular sensitivity and rising temperature is evidence of a severe toxic reaction. If vitamin B and 2,3-dimercaptopropanol (BAL) are to be used therapeutically, they must be given early, before irreversible pathological lesions have resulted.

The suggestion is made that BAL and vitamin B1, in adequate dosage, should be complementary in the treatment of arsenical encephalopathy. Intensive arsenotherapy is contraindicated when an initial pretreatment high level of pyruvic acid is found with clinical signs of subacute B1 avitaminosis.

—Bill Graham, '49.

V.D. CONTROL—STATISTICS
By Brown and Nichols

The authors report their analysis of the data received by the Division of V.D. Control, Ontario Department of Health. Of 5,032 notifications received by the department, 77.4% pertained to previously unreported infections and 22.6% were forwarded for other reasons. Physicians and clinics shared equally in providing 92.3% of notifications of previously unreported infections. Over 94.6% of the notifications supplied a full name.

The reported incidence rate, irrespective of sex or diagnosis, appears much higher in divorced or separated persons than in those who are married, single or widowed. Eighty-five per cent. of the reported primary and secondary syphilis among married persons was found after at least four years of marriage. In the divorced or separated group, all such diagnoses were made within four years of the stated date of separation.

The significant age groups for the acquisition of gonorrhoea and early syphilis are 20 to 29 years for men and 15 to 24 years for women.

The article concludes optimistically with the statement that current reported rates of venereal disease are as low as any over the past ten years.

—Britain Sanders, '48.

GLUMATIC ACID AND MENTAL FUNCTIONING

Zimmerman, Burgemeister and Putman
Psychosom. Med. IX, 175-183; 1947

The authors, who have previously presented a preliminary report on the effect of 1-glumatic acid, report their findings with 69 patients. Of these, 28 are children and adolescents with convulsive disorders, and 11 of the latter are also mentally retarded. Thirty-three are mentally retarded without convulsions. A control group was introduced to ascertain the effect of seizure reduction upon intelligence for varying periods of time and to determine the retest reliability of intelligence test scores.

The results indicate that glumatic acid accelerates mental functioning in human subjects and that this facilitation is a general effect, which is indicated in verbal, motor, and Rorschach tests.

The most striking changes appear in the seriously retarded group, where statistically significant differences are obtained between test and retest I.Q.'s. Greater improvement occurs in tests requiring abstract thought than on those involving motor skill; and emotional stability was improved in many cases.

Research is being continued to determine the ceiling effect of glumatic acid on intelligence.

—Paul Schneller, '49.