

5-1-1936

Differential diagnosis of coma

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THE
DIFFERENTIAL DIAGNOSIS OF COMA

AS

A PRESENTING SIGN

A Senior Thesis
by

Martin Frederick Anderson

April-1936

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INTRODUCTION

The terms "coma" and "comatose" refer to a state of complete loss of consciousness from which the patient cannot be aroused, even by the most powerful external stimuli, while "stupor" implies partial or nearly complete unconsciousness (13). Other terms, for example, deep coma or stupor, lethargic, unconscious, faint, "passed out", "in a swoon", have crept into the literature, serving only to confust the average reader. The writer shall interpret the terms "coma" and "comatose" according to Dorland's definition, thereby limiting the discussion to only those conditions wherein the unconscious patient cannot be aroused even by aggressive external stimulations.

Most of us have seen a patient in coma and have, perhaps, helped to determine the underlying cause. Few will disagree that the diagnosis often proves a difficult problem and that there is probably no other situation in which the doctor is called upon to so thoroughly "rake his convolutions" in an effort to make an early and correct interpretation of the mechanism producing the coma. And, although so many comatose states terminate fatally, in spite of correct diagnosis and treatment, early and accurate interpretation is essential if we are to save lives in those cases

requiring emergency treatment, for example: in traumatic shock, diabetes, insulin shock or hypoglycemia, poisoning, exsanguination, meningitis, subdural hematoma, and eclampsia. With the introduction of insulin and antitoxin serums, together with modern advances in brain surgery, additional weapons for combating coma have been given to the internist, and he no longer needs to stand by helplessly and wait for the inevitable end. Likewise, laboratory procedures, for the examination of the blood, urine, and cerebrospinal fluid, and the x-ray are valuable aids in the diagnosis of coma, without which numerous cases would be improperly diagnosed and improperly treated.

It would be well for all practitioners to acquaint themselves with an adequate knowledge of coma and its causes so as to enable them to quickly and accurately differentiate between various comatose states. Clinically, it is more important that the physician becomes thoroughly acquainted with some of the more common causes of coma rather than become confused in the attempt to master all known causes of coma.

It should not be difficult, however, for any student of medicine to acquaint himself with the majority of the causes of coma and to apply that correlated knowledge in solving what might appear to be a hopeless and entangled puzzle. It is the purpose of the author to acquaint the reader with certain fundamental principles, diagnostic rules,

and methods of procedure which will aid in the differential diagnosis of coma.

HISTORICAL

The earliest record of observations on patients during coma and following recovery is found in James Breasted's translation of the Edwin Smith Surgical Papyrus (8). The word "brain", recorded in human speech, appears for the first time. Breasted has conjectured that the original surgical treatise may possibly have been written by Imhotep, of the thirtieth century B. C., surgeon and royal medical adviser to the Pharaoh. The earliest discussion of the brain had hitherto been found in Greek medical documents, (34) probably over two thousand years later than our Egyptian treatise, which describes the brain as like the corrugations arising in the metallic slag,--an apt description of the convolutions of the brain.

The seat of consciousness and intelligence was from the earliest times regarded by the Egyptians as both the heart and the bowels or abdomen. Imhotep, however, observed the fact that injuries to the brain affected other parts of the body, especially the lower limbs. He noted the drag or shuffle resulting from a cranial wound. In this connection, the Egyptian surgeon made the extraordinary observations that the effect on the extremities shifted from side to side according to the side of the head which received the injury.

This is a recognition of the localization of function of the brain, although the ancient surgeon was apparently misled by a case of "contre-coup" regarding the side of the lower limb affected. Here then, is the discovery of the fact that the brain is the source of control of the movements of the body.

Francis Adams, (1) in his translation of the works of Paulus Aeginata, gives us proof of detailed observation of coma in the seventh century. Paul of Aegina (625-690 A.D.) discovered that when the common origin of the nerves, the brain, was affected, all the other parts of the body lost their motion and sensibility. The affection was called "apoplexy" by which the leading energies were impaired, but if the obstruction was in either side it was called hemiplegia and paralysis. Respiration was regarded as worst when it intermitted or was performed with great exertion. Paul of Aegina thought that the affection arose suddenly from a cold phlegm obstructing the most important cavities of the brain. If the sense of smell was affected, this arose from the anterior cavities of the brain or from the pores of the ethmoid bone being obstructed. Thus, apoplectics laid speechless, motionless, and insensible without fever. The precursors of this affection, Paul found, was sudden and acute pain in the head, distension of the jugular veins, vertigo, flashes, as it were, of light in the eyes, an inordinate coldness of the extremities, palpitation and difficult motion of the whole body and grinding of the teeth in sleep. The urine was small in quantity and of a greenish or black color. The affection

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occurred in old age in those of a phlegmatic temperament, and in those who used a diet of this nature. If it occurred in youth, it was in the season of summer and it indicated a strong exciting cause.

McDonnell, (28) in 1835, presented an article in which he discussed the physiology of coma. He felt that, "the physical condition of the brain" had not been given the importance which it deserved, and that, "a careful consideration of it would lead to valuable practical and physiological conclusions."

He felt that the brain was completely under the influence of the atmospheric pressure, and that comatose symptoms explained on the basis of brain compression, by practitioners, was paradoxical and absurd, and that in, "the great majority of these cases, compression of the brain had no concern whatever in the production of such symptoms". He based his conclusions on the following facts:

1. Many cases of so called brain compression failed to show any trace of evidence of the existence of compression on examination after death.
2. Deep sea diving animals (dolphin and the whale) descend to depths where the pressure is measured in "tons", and yet show no symptoms of brain compression.

- He was unable to explain how the comatose symptoms were produced by lesions usually looked upon as acting by compression, but he was convinced that the effect upon the circulation of the brain was an important factor, if not

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the cause itself of the symptoms of coma. He admits that, "any cause which considerably and suddenly diminishes the supply of blood to the brain" should lead to the development of comatose symptoms.

On the whole, McDonnell tries to impress his belief that the effect of atmospheric pressure is transmitted to the brain "as if the hemispheres were exposed naked". His observations were made with the view of calling attention to the physical condition of the brain, especially with reference to the circulation of blood in it, and to the presence of the atmosphere upon it. He failed to realize that many cases were, evidently, inaccurately diagnosed, and made the pathetic error of comparing himself with the dolphin and the whale. Such was the reasoning of McDonnell in the early nineteenth century!

George Johnson, (25) in 1869, presented the first real contribution to the study and diagnosis of coma. His lectures on the physiology of coma and anesthesia mark another milestone in the progress of medical science. For the first time, fact and opinion are strengthened by animal experimentation.

Johnson concluded that in all cases of unconsciousness resulting from disease or accident, or well designed experiment, the proximate cause in every instance was a suspended or diminished oxidation of the brain tissue.

His explanation of epileptic coma is interesting.

To quote:

"In epilepsy, as is now generally admitted, the loss of consciousness is immediately due to an arrest of the cerebral circulation, caused by a sudden and extreme contraction of the minute arteries of the brain. With the arrest of the oxygen bearing blood-stream there is an immediate suspension of the brain functions, and the phenomena of epilepsy are exactly imitated when death occurs from a rapid and copious hemorrhage, or when, in the lower animals, the arteries which supply the brain with blood are compressed or ligatured."

"In syncope", explains Johnson, "the heart's action is enfeebled, and the circulation ceases more or less completely, and in proportion to the degree in which the cerebral circulation fails, the functions of the brain, and especially consciousness, are suspended."

Concerning arterial and venous obstruction in the cereberum Johnson relates:

"While obstruction of the cerebral arteries causes anemia, and obstruction of the veins causes congestion of the brain, both the one and the other tend to suspend the functions of the brain, the essential cause of the suspended function in either case being, not the mere excess or deficiency of blood in the cerebral vessels, but the arrest of the blood stream through the capillaries."

Regarding coma from pressure on the brain--depressed fracture, tumor, or blood clot,--Johnson felt that coma was caused by an interruption of the cerebral circulation from pressure which was transmitted through the soft and yielding cerebral tissue, a mechanism for which the term "diaschisis" was suggested by Monakow(12).

In 1876, Sir David Ferrier, (16)the English neurologist, laid the foundation of knowledge concerning the localization of cerebral functions. He showed that the hemiplegias

and monoplegias, ensuing on injuries within the motor region of the ape, were characteristically greater than those produced by similar cerebral lesions in the dog. The symptoms in the ape he stressed as being strikingly akin to those familiar in the clinic. In 1884, (17) in collaboration with G. F. Yeo, he published a series of experiments concerning the effect of stimulation artificially produced in different regions of the cerebral hemispheres.

Macewen, (27) in 1879, was the first to record accurate observations concerning the condition of the temperature and the state of the pupils in comatose patients. From observations on fifty (50) cases of alcoholic coma he found that the temperature was consistently subnormal, ranging from 98.2° (rectal) to as low as 93.4° (rectal). But he was also aware of the fact that in apoplexy, opium poisoning and fractures of the skull, there was also found a subnormal temperature.

Macewen was the first to disprove the accepted belief that the pupils were dilated in alcoholic coma. He found that, contrary to the teachings of the time, forty-nine (49) out of fifty (50) cases of alcoholic coma had contracted pupils. Textbooks of that period infallibly stated that the pupils were dilated, but Macewen proved that the opposite condition existed. In the same forty-nine (49) cases he also noted that external stimuli caused dilatation of the pupils and that the pupils remained dilated for from ten to

twenty minutes, at the end of which time the pupils returned to their miotic state. He placed great stress on his pupil test. To quote:

"Given an insensible person, who has lain undisturbed for ten to thirty minutes, who then presents contracted pupils, which dilate on the application of external stimulation (without in any way arousing the patient) and which, if the person is left undisturbed, begin to contract again within a short time, I know of no other state to which this applies than alcoholic coma."

Charles Mercier, (31) in 1885, might be mentioned, in passing, as having submitted a test for coma which, he felt, was absolutely pathognomonic,--the movement of the eyes, independently of each other. To quote:

"It matters not what the cause of coma may be--whether alcohol, chloroform, ether, uremia, hemorrhage, a previous epileptic fit, a blow on the head, meningitis, cerebral tumor, or what not--if there is coma, the eyes move independently; if the eyes move independently, there is coma."

Esqueridge, (14) in 1898, submitted the first extensive discussion on the differential diagnosis of coma as well as a classification for the various causes of coma. His classification will be found in the chapter on "Classification of Coma."

Forsythe, (18) in 1912, further contributed to the study and diagnosis of coma by discussing the significance of various clinical findings. He was probably the first writer to suggest a definite coma routine. Although incomplete, compared to those submitted by more recent writers, (5)(20) it is interesting to note that he favored four special inves-

tigations: the urine, fundoscopic examinations, lumbar puncture, and analysis of the gastric contents. He also submitted a classification for the causes of coma, and discussed the differential diagnosis of various types of coma.

Harvey Cushing, (39) in 1907, took advantage of the exceptional opportunities afforded by operations upon the human brain, for analysis of function, especially when carried out under local anesthesia (a procedure which he was the first to introduce). As a pupil in Sherrington's laboratory at Liverpool, he assisted in the experiments on stimulation of the motor area of the higher apes. Soon afterwards he made corresponding observations on human beings under surgical anesthesia (42). The story of his first experience in stimulating the motor and sensory areas of a conscious patient is related in his article published in 1908 (39).

Cushing established convincingly, by human experiment, that the reactions studied in higher apes were applicable to human beings and provided, for the first time, direct evidence that irritation of the postcentral gyrus gave rise to sensation; a fact which could not be established by experiments on animals.

CLASSIFICATION OF COMA

Although coma has been discussed rather freely by numerous writers, only a few have attempted to submit some sort of a classification of the various causes. Perhaps there is no single classification which can include all of the possibilities since many of the causes could be included under more than one group or subgroup. Only four references on this phase of the subject were found worth mentioning.

The earliest classification was that offered by Eskeridge in 1898(14), who divided the causes of coma into seven groups, excluding those of hyperpyrexia, typhoid fever, cancer in portions of the body other than the brain, and from acute yellow atrophy of the liver. His classification is as follows:

- I. Transient coma.
 1. Syncope as in fainting.
- II. Coma from lethal doses of medicinal agents.
 1. Chloral
 2. Opium
 3. Belladonna
 4. Hyoscyamus and its alkaloids
 5. Alcohol
 6. Lead
- III. Coma from poisons other than medicinal agents circulating in the blood.
 1. Asphyxia from poisonous gases
 2. Ptomaines
 3. Uremia
 4. Diabetes.

- IV. Convulsive states preceeding coma
 - 1. Pre-eruptive stages of the exanthemata
 - 2. Reflex convulsions, such as teething, overloaded stomach, etc. in children.
 - 3. Epilepsy
 - 4. Hysteria
 - 5. Epileptoid and apoplectoid attacks due to paretic dementia, or other organic brain disease, such as syphilis and chronic alcoholism.

- V. Voluntary coma
 - 1. Feigning

- VI. Coma from profound disturbances of the cerebral circulation, but unattended by organic lesions of the brain substance.
 - 1. Shock
 - 2. Concussion of the brain
 - 3. Congestion of the brain
 - 4. Anemia of the brain

- VII. Coma from organic disease of the brain
 - 1. Simple "apoplexy" of the aged
 - 2. Traumatism of the brain.
 - 3. Syphilis of the brain
 - 4. Cerebral meningitis
 - 5. Abscess of the brain
 - 6. Tumor of the brain
 - 7. Cerebral hemorrhage
 - 8. Cerebral embolism
 - 9. Cerebral thrombosis

Scientific knowledge concerning coma was apparently not overly abundant during Esqueridge's period. McDonnell(28) in 1835 called attention to the "physical condition of the brain, especially with reference of circulation of blood in it, and to the presence of the atmosphere upon it". Johnson (25) in 1869, struck a keynote when he concluded, "the proximate cause in every instance is a suspended or diminished oxidation of the brain tissue". Mercier, 1885, described coma as consisting of four (4) stages, wherein the successive loss of functions of the nervous centers took place in the

order from the highest to the lowest (31).

Forsythe, in 1912, outlined the causes of coma into three main groups:

- I. Derangement of cerebral circulation
 1. Vascular derangements of the brain
 - a. Hemorrhage
 - b. Thrombosis
 - c. Embolism
 2. Injuries to the head
 3. Epilepsy
 4. Diabetes
 5. Poisons
 6. Stokes-Adams disease
- II. Coma culminating illnesses
 1. Meningitis
 2. Encephalitis
 3. Cerebral abscess
 4. Cerebral tumor
 5. Fevers
 6. Eclampsia
 7. Cholemia
 8. Epidemic enteritis
 9. General Paralysis
 10. Disseminated Sclerosis
- III. Miscellaneous
 1. Pernicious malaria
 2. Muscle exhaustion
 3. Heat stroke

Herbert French, (21) in 1917, classified the causes of coma into two main groups: A and B.

Group A. Cases in which coma is not a prominent symptom early in the malady, but only in a late stage, when the nature of the disease has already been suggested by other symptoms.

- I. Certain severe fevers
 1. Typhus fever
 2. Typhoid fever
 3. Cholera
 4. Dysentery
 5. Measles
 6. Scarlet fever
 7. Rheumatic fever
 8. Yellow fever

9. Blackwater fever
10. Malignant malaria
11. Infective endocarditis
12. Diphtheria

II. Acute Inflammatory lesions of the brain or the cerebral meninges.

1. Acute encephalitis
2. Suppurative meningitis
3. Tuberculous meningitis
4. Posterior basal meningitis
5. Epidemic cerebrospinal meningitis or spotted fever

III. Certain less acute lesions of the central nervous system

1. Cerebral tumor
2. Cerebral abscess
3. Post-epileptic state
4. General paralysis of the insane
5. Disseminated sclerosis
6. Syphilis of the brain

IV. Diseases in which general metabolism is probably at fault.

1. Uremia
2. Diabetes
3. Cholemia
4. Addison's disease
5. Raynaud's disease
6. Myxedema

Group B. Cases in which coma comes on early and may be the most prominent feature of the case.

I. The results of head injury.

1. Compression of meningeal hemorrhage
2. Concussion
3. Depressed fracture
4. Fracture of the base of the skull

II. Vascular lesions of the brain.

1. Embolism
2. Hemorrhage
3. Thrombosis
 - a. Arterial
 - b. Of a venous sinus such as the superior longitudinal

III. The acute effects of drugs

1. Alcohol
2. Opium
3. Morphia

4. Carbolic acid
5. Oxalic acid
6. Carbon monoxide
7. Absinthe
8. Chloral hydrate
9. Veronal
10. Sulphonal
11. Trional
12. Tetronal
13. Bromides
14. Chloroform, and other anesthetics.

IV. The chronic effects of chemicals

1. Saturnine encephalopathy

V. The effects of extremes of temperatures

1. Heat stroke
2. Excessive cold

VI. Excessive loss of blood from:

1. Ruptured tubal gestation
2. Post partum hemorrhage
3. Hemoptysis
4. Hematemesis
5. Duodenal bleeding
6. Intestinal bleeding
7. Ruptured aneurysm

VII. Stokes-Adams disease

VIII. Sudden nervous shock

IX. Hysterical trance

E. D. Friedman, 1933, (20) was much more conservative.

He groups the various causes of coma under four headings:

I. General

1. Alcoholism
2. Uremia
3. Diabetes
4. Opium
5. Gas Poisoning
6. Hypoglycemic states

II. Epilepsy

III. Intracranial lesions with or without focal signs

1. Apoplexy
2. Meningitis

3. Abscess of the brain
4. Tumor of the brain
5. Encephalitis
6. Spontaneous subarachnoid hemorrhage

IV. Trauma

1. Concussion of the brain
2. Gross hemorrhage with or without fracture.

Friedman's classification may seem less complete than that of French, but it is far more practical to the average practitioner. To construct a complete and thorough outline of all the causes of coma would be a difficult undertaking. Regardless of the plan of outline, there would always probably be a final group, frequently referred to as "miscellaneous".

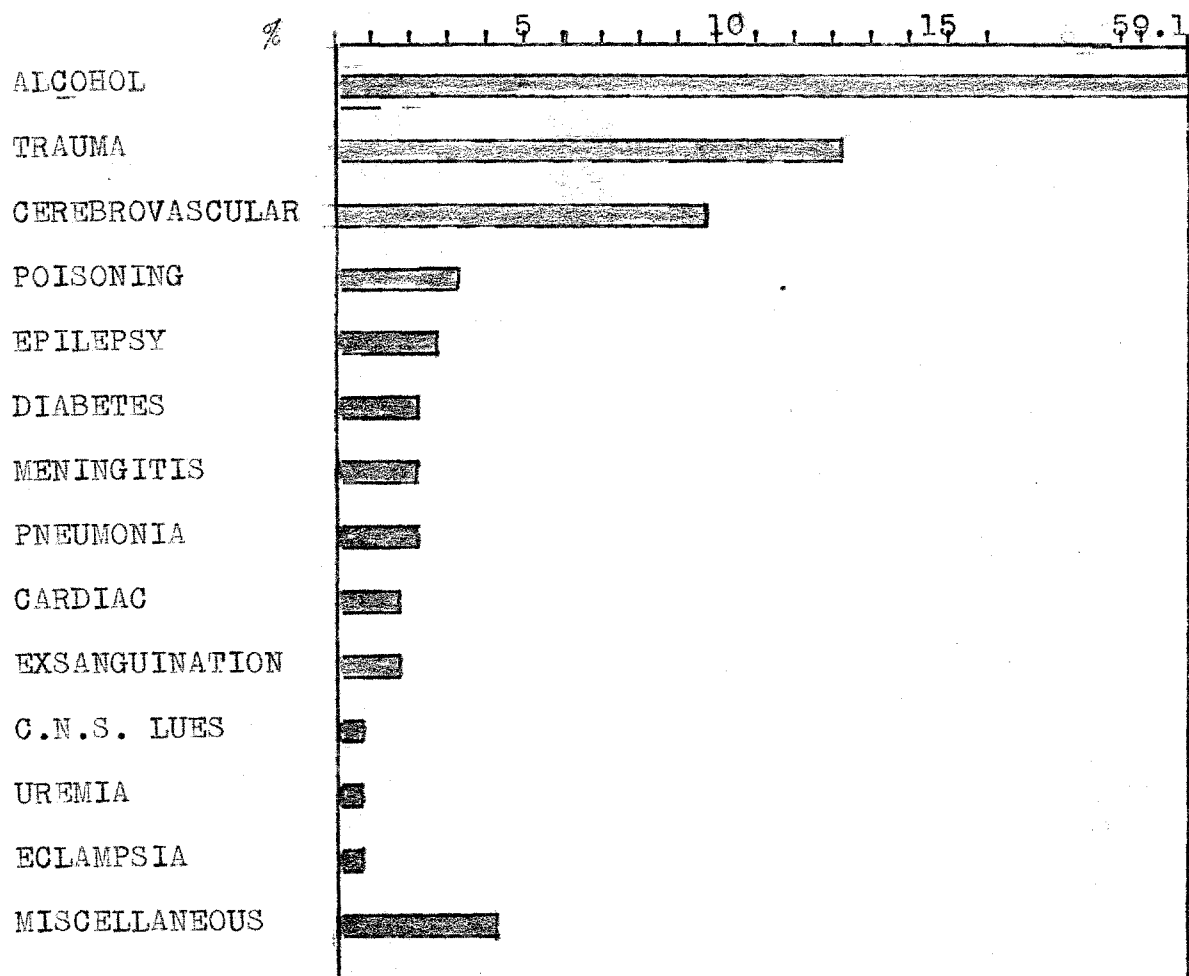
It is interesting to note that no outline as yet has been thorough enough to include all causes of coma. Such a classification would be interesting from an academic viewpoint, but probably impractical clinically. According to Friedman, determination of the cause of unconsciousness is the important factor since treatment is dependent upon it. Consequently, a knowledge of the more common causes and the ability to recognize and interpret items of value are to be emphasized if one wishes to develop diagnostic acuity.

RELATIVE FREQUENCY OF THE CAUSES OF COMA

A knowledge of the more common causes of coma, as a presenting sign, as well as the relative frequency with which they occur, is of far more value in the diagnosis of coma than the average diagnostician realizes. The literature contains very little data on coma statistics. Camauer(11) published an analysis of twenty-six (26) cases. Bissell and LeCount(6)(7) analyzed the causes of death in four hundred (400) patients who died in coma, and Holcomb(23) continued the analysis with an additional three hundred and forty-six (346) cases.

Cases coming to autopsy, where death was due to coma, represent but a small percentage of the total number of cases of coma. And, also, many cases develop coma in the hospital as a terminal state. Consequently, Bissell and Le Count's and Holcomb's statistics are not applicable to the problem of coma as a presenting sign. These authors have prepared in chart form, in order of their frequency, the causes of coma as determined by post mortem examination. The reader is referred to the original articles for complete statistics concerning that phase of the subject.

The textbooks(12)(33)(41) are of little or no assistance. They mention many causes of coma and discuss at length some that are very uncommon, while other causes that are more



Causes of coma on admission to the hospital, 1167 cases.

Figure 1.

common are not included at all. They do not attempt to classify the causes according to their relative frequency, with exception of Barton and Yater (4) who divide the causes of coma into the common and less common causes.

Solomon and Aring (35) reported a summary of 1167 patients entering the hospital in coma. All cases were analyzed and the diagnoses arrived at were tabulated in the order of their frequency. Of these 1167 cases, alcohol was responsible in 59.1%; trauma in 13%; and cerebral vascular lesions in 10%. The last two made up more than one fourth of the non-alcoholic comas. Other causes, each forming 3% or less of the total in order of numerical importance were: poisoning, epilepsy, diabetes, meningitis, pneumonia, cardiac decompensation, exsanguination, syphilis of the central nervous system, uremia, and eclampsia. Figure 1 shows schematically, the causes of coma arranged according to the relative frequency of their occurrence.

Among the traumatic cases, injuries to the head were by far the most common. Of the head injuries there was a high proportion of subdural and extradural hematomas. Figure 2 lists the various types of trauma arranged in the order of their numerical importance. In the cases where alcoholism was associated with severe head injuries, the coma was listed under head injuries with alcohol considered as a secondary factor.

In analyzing the types of cerebral vascular lesions, the same authors found that cerebral hemorrhage was most com-

Type	Number of cases	Cases with fractured skull	% with fractured skull
CONCUSSION	17	0	0
EDEMA OF BRAIN	20	3	15
CONTUSION OF BRAIN	38	9	24
LACERATED BRAIN	47	41	87
SUBDURAL HEMORRHAGE	12	4	33
EXTRADURAL "	3	2	67
TOTAL HEAD INJURIES	<u>137</u>	<u>59</u>	<u>43</u>
CHEST INJURIES	7		
PELVIC INJURY	4		
SPINAL CORD INJURY	<u>4</u>		
TOTAL	152		

Fig. 2. Coma due to trauma.

Type	Number of cases	% of cerebral vascular lesions
HEMORRHAGE	49	42
THROMBOSIS	29	25
HYPERTENSIVE AND ARTERIOSCLEROTIC ENCEPHALOPATHY	10	8
EMBOLUS	5	4
PRIMARY SUBARACHNOID HEMORRHAGE	4	3
UNDETERMINED	<u>21</u>	<u>18</u>
TOTAL	118	100

Fig. 3. Coma due to cerebral vascular lesions.

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on. Diagnoses were based on autopsy findings or by the presence of gross blood in the spinal fluid. There is reason to believe(3) that in cerebral vascular lesions, with or without coma, cerebral thrombosis is more common than cerebral hemorrhage. Coma as a presenting sign favors hemorrhage as against thrombosis, while the absence of coma is in favor of thrombosis. Figure 3 illustrates the frequency of various types of cerebral vascular lesions as determined by Solomon and Aring.

Diabetic coma is not as frequent as in the pre-insulin period but even today it is not rare. Many are precipitated by acute upper respiratory infections. Pneumonia is not mentioned in the textbooks as one of the causes to be considered in which coma is a presenting sign. Yet pneumonia was three times as frequent as uremia in Solomon and Aring's series. The relatively few cases of uremia in the above series is not in keeping with the supposedly more common causes of coma. Many more patients develop uremic coma terminally while in the wards. It would seem that kidney insufficiency in more instances should be gradual enough in onset and should produce enough symptoms to bring the patient to the hospital before coma supervenes. In the miscellaneous causes of coma, the rarity of cholemia, Stokes-Adams disease, syncope, and hysteria as causes of hospital admission in coma is noteworthy.

THE CLINICAL SIGNS AND MANIFESTATIONS OF COMA

The many signs, symptoms, and findings of coma are as numerous as are the causes themselves and, yet, they are not too numerous to escape discussion of their individual values for the part they play and the help they render in arriving at a solution to the problem before us. Unfortunately, too many of the phenomena are diagnostic of more than one cause of coma. This is what determines their value.

It has been interesting to note the manner in which writers were prone to accept opinions rather than facts and how these opinions have crept into the literature. A good example of this type is the "fable" concerning the dilated pupils of alcoholic coma. Practically every text book or article on coma mentions this sign and yet Macawen, as early as 1879, proved conclusively, that in 49 cases out of 50 cases of alcoholic coma, the pupils were contracted, dilating under the influence of external irritation, only to resume their miotic form after cessation of the stimulus.

In the present chapter, the writer shall attempt to bring under discussion the more important findings which are often present in comatose patients but which are often overlooked because the observer fails to hunt for them or,

not finding them present on the first examination, neglects to look for them on successive observations.

The order of discussion automatically becomes one of three possibilities: first, according to the frequency with which they are found; secondly, according to the value of their significance; and thirdly, in the order according to the anatomical systems of the body. It would be difficult to follow the order of the first. The order of the second would be logical enough, since there are some signs which occur in only one or two conditions and are diagnostic of those one or two conditions. In the opinion of the writer, it seems more logical to follow the order of the third, i.e., to begin with the head and proceed downward in orderly fashion, ending with the extremities and the reflexes. This is the usual order of physical diagnosis which has been taught by the medical colleges and is the accepted method today (43)(41).

Observation of the patient. As Forsythe (18)¹⁸⁴² states:

"Depend upon it, the patient, unconscious as he is, has after all, a tale of his own to tell"

To quote Spriggs:

"If young, think of the possible causes of coma in young adults; epilepsy, embolism, trauma. If young and thin, with dry skin, think of diabetes. If elderly, and full blooded, apoplexy should be suspected."

Color of the skin. Most writers mention the "cherry red" color of carbon monoxide poisoning (4)(36); the flushed

skin of alcoholism(12)(36); and the cyanosis of cardiac decompensation(12)(33)(36).

Convulsions. Considerable significance was attached to convulsions, although few attempts were made to differentiate between the various types of convulsions, i.e., clonic, tonic, or muscle twitchings. Spriggs differentiated between epilepsy and uremia, but said nothing of cerebral vascular lesions or syphilis, while Forsythe emphasized paresis and multiple sclerosis. To quote Forsythe:

"a convulsion leading to coma may be the first smoke from the fire, rising long before suspicion would otherwise have been aroused. This prognostic is, perhaps, not always borne in mind when a patient, man or woman, previously healthy, is taken with an apparently inexplicable convulsion."

Solomon and Aring(36)mention the possibility of epilepsy, cerebral vascular lesions, central nervous system syphilis, and alcoholism. If the patient is a female within the child bearing age, and signs of pregnancy are evident, eclampsia should immediately be suspected.

Earlier writers(37)(18)advise determination of the depth of coma first. Von Wedekind's test of supra-orbital pressure was mentioned as a test of coma by Spriggs:

"Von Wedekind, in 1882 (Lancet), stresses the value of supra-orbital pressure in quickly making a diagnosis of alcoholic coma. Lack of response to pressure denotes coma from some other cause."

The writer has seen this same test used clinically in addition to "pinching the skin" or bringing a hot object close to the body.

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Gowers (22) has pointed out that the manifestations in a comatose patient depend on the depth of coma, whatever the cause may be. Solomon and Aring (36) agree with Gowers in this respect. According to their experience, if the coma is light, the reflexes may be hyperactive, perhaps because of release of the lower centers by lack of cerebral control.

Respiration. This will be found to be quite variable in coma. Spriggs mentions nine possibilities, differentiating between "stertorous," "shallow and sighing," "slow and deep," and "quicker and noisy." A more recent article (36) mentions the value of Kussmaul's breathing in diabetic coma, and rapid respiration in pneumonic coma. Greater significance of any particular type of respiration depends more upon other accompanying signs of value.

Muscular twitching. Solomon and Aring mention this as occurring only in uremic coma. Earlier writers fail to mention this valuable diagnostic sign, unless perhaps they improperly referred to it as "convulsions."

Temperature. The temperature, also, unfortunately, can be rather variable, and this detracts from its value, but there are a few characteristics of the temperature which make it necessary to keep it in mind when putting together "the whole picture."

Macewen (27), in 1879, found that the temperature was constantly below normal in alcoholic coma, but he was also aware of the fact that subnormal temperatures were common in

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opium poisoning, apoplexy and fracture of the skull.

Feiling (15), in 1934, placed not a little significance on the rapid appearance of fever together with respiratory paralysis, in cerebral hemorrhage. Aring and Merritt (1935) (3) found that a practically constant finding in any type of cerebral vascular lesion was the uniform rise of temperature, pulse rate, and respiratory rate several hours or days before death occurred, indicating a collapse of the vasomotor and heat regulating centers.

Solomon and Aring (1935) (36) found that a rise in temperature was common in coma due to pneumonia, meningitis, or encephalitis; while a decrease in temperature was more apt to be found in carbon monoxide poisoning and diabetes.

In the examination of the patient all sorts of plans are advocated. One writer will emphasize the value of certain eye signs as valuable criteria in the diagnosis of coma (24) (30), while another the value of heart and pulse (36).

The importance of the eye as an aid to the diagnosis of coma has been mentioned, in practically all articles on coma. The familiar "pin point" pupils of opium poisoning and the "Hutchinson" pupil of a unilateral brain lesion with compression, are quite frequently mentioned, although Solomon and Aring, in a very recent article, felt that the depth of the coma, condition of the pupils, and the state of the reflexes were not of great diagnostic importance. The author feels that additional space should be devoted here to a

short review concerning the part the eyes may play in comatose patients.

For historical interest only is an article by Mercier in 1885, discussing a test for coma. The inaccuracy of the physicians of that time, whether because of lack of cases seen or failure to observe is illustrated by Mercier's bold but unfounded statement:

"It matters not what the cause of coma may be-- whether alcohol, chloroform, ether, uremia, hemorrhage, a previous epileptic fit, a blow on the head, meningitis, cerebral tumor, or what not--if there is coma, the eyes move independently; if the eyes move independently, there is coma."

But the conspicuous inaccuracy of Mercier's observations was more than offset by a brilliant piece of work carried out by Macewen who, in 1887, found that a dilated and fixed pupil signified serious brain injury. To quote Macewen:

"when the functions of one half of the cerebrum is placed in abeyance by a superficial or cortical lesion, the pupil on the same side as the lesion is in a state of stable mydriasis."

Macewen fortified his claims by quoting results from private observations, checked by postmortem findings in fatal cases. This should be considered as an exceptionally fine piece of work coming as early as 1887. Incidentally, it was Macewen, who, in 1879, disproved the fable of "Dilated pupils in alcoholic coma."

Spriggs, in 1904, mentioned the value of a unilaterally dilated and fixed pupil on the side of compression, referring to the phenomena as "Hutchinson's pupil". Later

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writers, Haesly (1919) (9), Brooks (1921) (9), Holm and Scott (1925) (24), and Menninger (1927) (30) also refer to the value of the "Hutchinson pupil" as an aid in determining the location of intracranial injury of hemorrhage.

Brooks (1921) (9), in discussing the significance of unequal pupils, concluded:

1. With the exclusion of eye disease and refractive errors, unequal pupils are always pathologic.
2. The width of the pupil and its reaction are a result of constant antagonism between the contracting fibers of the third nerve and the dilating fibers of the cervical sympathetic.
3. The determination of whether we are dealing with an irritating or paralytic lesion will help in the recognition and proper interpretations of unequal pupils in any case.
4. In head injuries, the dilated pupils corresponds to the side of increased pressure.

Although Brook's observations do not apply strictly to patients in coma, his principles, nevertheless, are worth applying when interpreting and evaluating unequal pupils in comatose patients.

Kearney, in 1922, stressed the value of fundoscopic examination following head injuries or in cases suspected of having increased intracranial pressure, attaching little or no importance to gross signs. To quote: (26)

"Pupillary changes, per se, were found of small value as an indication of excess intracranial pressure or localization of the seat of injury, but they have been an aid, at times, when taken into account with the entire clinical picture."

Holman and Scott (24), in 1925, stressed the value of the "Hutchinson pupil" in severe skull injuries and cri-

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ticized Kearney's statement concerning the value of pupillary changes per se. They reported eight cases in which the pupil was present. Hemorrhage or hematoma on the corresponding side of the dilated and fixed pupil was verified by operation or necropsy. In two of the cases there were bilateral pupil signs. Necropsy on the one showed both lateral ventricles distended with blood. A bilateral decompression was necessary in the second case, followed by recovery, but complicated by later mental changes. Some valuable points are stressed by Holman and Scott in their comment:

"We believe the frequent and accurate observation of pupils in patients who become unconscious as a result of head injuries to be very important, as they may be a valuable aid in determining the side on which the operation for the relief of intracranial hemorrhage should be performed."

The importance of the sign makes it imperative that its appearance be not prevented by the use of homatropin or other mydriatic drugs following skull injuries.

In conclusion, Holman and Scott formulated four important rules:

1. Unilateral dilatation and fixation of the pupil is a valuable aid in determining the location of the intracranial injury and hemorrhage following head injury.
2. Operative intervention should be directed toward the side on which the dilatation and fixation first appear.
3. Its transitory character makes accurate and off-repeated observations necessary from the moment of injury.
4. The use of mydriatics should be avoided when intracranial trauma and hemorrhage are suspected following severe head injuries.

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Meninger (30), in 1927, made a very excellent and exhaustive review of the literature concerning the "pupils as an aid to diagnosis". He also analyzed 225 cases of coma with regard to pupillary status, including equality, size and reaction to light.

The entire subject concerning pupillary signs is very well summarized by Meninger in his conclusion:

"Pupils may be an aid in diagnosis of comatose states resulting from brain trauma (hemorrhage or pressure). They are of little or no diagnostic importance when the coma is due to alcoholic poisoning, diabetes, uremia, or carbon monoxide."

In 46 cases of cerebral hemorrhage, nearly three fourths or 73.9% showed anisocoria. The dilated pupil usually occurred on the side corresponding to the hemorrhage, but this depended on the location and extent of the hemorrhage. In five cases of pontine hemorrhage, all were uniformly contracted, and either very sluggish or fixed to light.

In fifty-five cases of fractured skull anisocoria occurred in over one third or 37.8% of the cases; in 81% of these there was either proof or evidence that the dilatation occurred on the side of the brain trauma.

Friedman(19), in 1919, introduced his sign, "unilateral anesthesia of the cornea and conjunctiva" as a diagnostic sign of coma due to hemiplegia. He admits that in deeply comatose patients, all reflexes are usually absent, and that the sign would be more valuable in cases of

of light coma and stupor. He never observed the sign in a case of crossed paralysis. He realized that a fracture of the skull, involving the posterior fossae, would complicate the picture and give false results because of injury to the Trigemini. None of the other writers mention Friedman's test, although Friedman himself, felt that his sign was especially valuable for the ambulance surgeon as an aid in differentiating alcoholism from hemiplegia.

In regard to the tongue, there are two rather definite and specific conditions which, if found, are almost always pathognomic of the diseases in which they are so commonly found. The first of these,--the "scarred" or bitten tongue,--practically always signifies epilepsy. The second,--"deviation or protrusion,"--is a sign of paralysis of the side to which the tongue is retracted.

The frequently mentioned "stiff neck" or "retracted head" is diagnostic of cortical irritation and may be found in meningitis and cerebral vascular lesions. It is needless to mention here the numerous writers who have used this valuable sign.

Chest signs may be limited to two: consolidation and fluid. The former is diagnostic of pneumonia. The latter, according to Solomon and Aring(36), is suggestive of empyema or ruptured aortic aneurysm. Any lagging of one side of the chest might also be mentioned here as being suggestive of hemiplegia.

Examination of the heart may disclose several valuable clues. The detection of a murmur in a young adult may lead to a diagnosis of embolism. An irregular pulse should make one suspicious of a decompensated and failing myocardium. A slow pulse, from 30-40, is indicative of Stokes-Adams disease. And a rapid pulse may accompany any one of a half dozen conditions: pneumonia, meningitis, diabetes, and eclampsia. Increase in blood pressure is more valuable when considered in conjunction with other signs, but is frequently found in cerebral vascular lesions, uremia, and eclampsia.

An abdominal tumor may suggest eclampsia, while ascites, with liver enlargement, would lead one to suspect cardiac decompensation. Distention and spasticity of the abdominal musculature would necessitate the verification of or the ruling out of ruptured ectopic pregnancy, miliary tuberculosis or other probably abdominal pathology.

The value of the reflexes is praised by some writers (15)(24) and doubted by others (26)(36). It is true that the state of the reflexes is dependent upon the depth of the coma (22)(24)(41) but, when present, the reflexes may have great bearing upon the final diagnosis. Thus any inequality of the reflexes, or the absence of reflexes on one side only is diagnostic of hemiplegia and should immediately suggest a cerebral vascular lesion of the opposite side (15). The Babinski sign is pathognomonic of a pyramidal tract lesion. The value of the signs of hemiplegia is increased when ac-

Lumbar puncture

Pressure

Increased.....cerebral vascular lesions; meningitis;
trauma; syphilis of the central nervous system

Decreased.....diabetes

Bloody fluid.....cerebral vascular lesions; trauma

Purulent fluid.....meningitis

Organisms by smear and culture.....meningitis

Sugar

low.....meningitis

high.....diabetes

Protein high.....meningitis; syphilis of the central nervous system

Spinal fluid Wassermann positive.....syphilis of the central nervous system

Blood examination

Sugar

high..... diabetes

low insulin shock

Nonprotein nitrogen high.....uremia

Wassermann test positive.....syphilis of the central nervous system

Low red blood count, abnormal smear....pernicious anemia
leukemia

Culture positive.....pneumonia, meningitis, septicemia

Spectroscopy.....carbon monoxide poisoning
methemoglobinemia

Urine examination

Sugar.....diabetes

Gross albuminuria.....eclampsia, uremia, cardiac decompensation

Gastric lavage; examination of gastric contents,.poisoning

Roentgenograms

Skull.....fracture across middle meningeal artery
in extradural hemorrhage

Lungs.....pneumonia; empyema; miliary tuberculosis

Heart..... cardiac decompensation

Electrocardiograph heart block; cardiac decompensation

Fig. 4. Laboratory Observations Helpful in
the Diagnosis of Coma and the Conditions
in Which They Occur.

Odor of breath	
Alcohol.....	alcoholism
Acetone.....	diabetes, uremia
Illuminating gas.....	carbon monoxide poisoning
Color of skin and mucous membranes	
Hyperemic.....	alcoholism
Cherry red.....	carbon monoxide poisoning
Cyanosis.....	cardiac decompensation, pneumonia
Pallor.....	hemorrhage, pernicious anemia
Jaundice.....	cholelithiasis
Local signs of injury.....	trauma, burns, hemorrhage, epilepsy, erysipelas
Temperature	
Increased.....	pneumonia, meningitis, encephalitis
Decreased.....	carbon monoxide poisoning, diabetes
Pulse	
Rapid.....	diabetes, pneumonia, meningitis, eclampsia
Irregular.....	cardiac decompensation
Slow.....	opium, Stokes-Adams disease
Respiration	
Kussmaul.....	diabetes
Increased.....	pneumonia
Slow.....	opium
Hemiplegia.....	cerebral vascular lesions
Observation of convulsions.....	epilepsy, cerebral vascular lesions, central nervous system syphilis, alcoholism
Vomiting.....	cerebral hemorrhage, poisoning
Stiffness of the neck.....	meningitis, cerebral vascular lesions
Kernig's leg sign positive....	meningitis, cerebral vascular lesions
Chest signs	
Consolidation.....	pneumonia
Fluid.....	empyema, ruptured aortic aneurysm
Pulmonary congestion, ascites, enlarged liver, distended neck veins.	cardiac decompensation
Distention and spasticity of the abdomen.....	ruptured esophageal varix, carcinomatous erosion of the gastro-intestinal tract, ruptured ectopic pregnancy, miliary tuberculosis
Muscular twitchings.....	uremia
Abdominal tumor.....	eclampsia
Bulging fontanel.....	meningitis
Soft eyeballs.....	diabetes
Wounds or scars on tongue.....	epilepsy
Vaginal examination abnormal....	pelvic malignancy, ruptured ectopic pregnancy
Blood pressure	
Increased.....	cerebral vascular lesions, uremia, eclampsia
Decreased.....	trauma

Fig. 5. Physical Changes Helpful in the Diagnosis of Coma and the Conditions in Which They Occur.

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companying signs can be discovered. In a young patient, suspect embolism, and examine the heart. In an older patient suspect apoplexy. In any patient think of the various types of brain lesions and differentiate between them.

The various laboratory procedures and their significance have been summarized by Solomon and Aring in fig. (4).

The same authors have briefly outlined the physical changes helpful in the diagnosis of coma, and the conditions in which they occur. The writer is indebted to them for the outline in fig. (5), modified, somewhat, in order to make it more complete.

DIFFERENTIAL DIAGNOSIS

The diagnosis of coma is not a new subject, and it is not the purpose of the writer to replace the few well written papers discussing coma with a faultless or fool proof logic but rather to summarize and analyze the more important literature which will contribute to the knowledge necessary to aid in the differential diagnosis of coma where coma is the presenting symptom.

Little help is obtained from textbooks (12) (33) (41) which discuss the subject in a too general and abstract manner. A few authors, however, have attempted to aid the practitioner in the diagnosis of coma of unknown cause (14) (18) (34). A recent article by Solomon and Aring very ably discusses the problem of diagnosis (36) while a more recent paper by Straus and Binswanger (38) excellently discusses coma from the standpoint of immediate and proper treatment.

Just as so many authors have emphasized, there are not a few causes of coma which require early emergency treatment to save life, for example: diabetes, hyperinsulinism, poisoning, exsanguination, eclampsia, traumatic shock, subdural hematoma, meningitis, and brain tumor. The importance of early and accurate diagnosis is self-evident.

In discussing the diagnosis of coma, the writer will attempt to follow the order of frequency as already described in a previous chapter. They busy practitioner will appreciate this line of attack

for reasons heretofore mentioned. The knowledge concerning the relative frequency of the causes of coma, alone, is of considerable worth and may have an important bearing on the differentiation of coma in numerous instances.

The present chapter is a critical analysis of the causes of coma with the purpose of determining criteria which will aid in the diagnosis of coma. In many instances, fortunately, a history will be obtained. This often will greatly simplify or at least verify the diagnosis. In presenting the chief diagnostic criteria of each of the causes of coma, the history will frequently be mentioned. The essential parts of the history affecting the case will be emphasized. Otherwise, the writer will assume that no history is obtainable and will mention only those points of enough significance to make their consideration worthwhile as an aid in diagnosis of coma.

The following is a discussion of the more significant diagnostic criteria.

Coma due to alcoholism. The typical patient in alcoholic coma has a flushed face, injected throat and conjunctivae, diminished or absent reflexes, and an alcoholic odor to the breath. Vomiting is not uncommon and, according to Solomon and Aring, (36) convulsions occasionally occur. In fatal cases the coma is more complete from the outset, and convulsions more common. In such cases the physical examination of the patient is likely to show signs of further abnormalities such as cyanosis, cardiac hypertrophy, heart sounds irregular and of poor quality, pulmonary rales, low blood pressure, and increase in white blood count or non-protein nitrogen.

Macewen (27) mentioned the value of a subnormal temperature.

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In fifty (50) cases of alcoholic coma he found temperatures ranging from 93.4° (rectal) to 98.2° (rectal). Unfortunately, other causes such as apoplexy, opium poisoning, and skull fracture may cause considerable lowering of the body temperature, and must be considered in the differential diagnosis.

Concerning the condition of the pupils in alcoholic coma, Macewen (27) found that in 49 out of 50 cases the pupils were contracted, but that external stimulation caused a dilatation which lasted for from ten to twenty minutes, following which period the pupils returned to their original miotic state. Meninger (30) on the other hand, after a complete analysis of 225 cases of coma in regard to pupillary status, concluded that pupillary signs were of little or no diagnostic significance when coma was due to alcoholic poisoning.

According to Strause and Binswanger, (38) the alcoholic breath is, in itself, of little value, but if an attendant makes the statement that the patient never drank or the opposite statement, that the patient is a confirmed drunkard, much diagnostic help is obtained.

Differential Diagnosis

Apoplexy occurs in elderly patients. There is usually a history of sudden onset of coma. Signs of paralysis are usually present or develop in the course of events. The pupils are markedly contracted in pontine hemorrhage. Unequal pupils are frequently found. A sudden rise in blood pressure and temperature is diagnostic, but carries a very bad prognosis. If conjugate deviation of the eyes is present, the patient most commonly "looks at his lesion". A lumbar puncture is especially valuable in cerebral hemorrhage, revealing a grossly bloody spinal fluid.

Opium poisoning will give "pin point" pupils and a subnormal temperature. The respirations are characteristically slow and irregular. The breathing is frequently stertorous and the odor of opium may be detected on the breath. The pulse is slow and easily compressible. The skin is cold and moist,

and cyanosis is the rule rather than the exception. Gastric lavage will verify the diagnosis in many cases.

In skull fracture there is a history of injury or evidence of trauma. The presence of blood or spinal fluid coming from the nose or ears or the presence of bruises and hematomas should lead one to immediately suspect trauma. X-ray of the skull should always be performed in suspicious cases.

Coma due to trauma

Solomon and Aring (36) obtained a history of trauma in 90% of their cases. The apparent condition of the patient usually gives one a clue as to the circumstances of the case. Physical examination will give evidence of injury, the degree of which may be determined by roentgenograms, and lumbar puncture. The frequent recording of temperature may be of value.

Differential Diagnosis

In concussion, according to Trotter (40), the diagnosis should always be easy. In a well marked case the three elements of

1. The instantaneous onset.
2. The paralytic nature of its symptoms, and
3. The tendency to recover spontaneously are characteristic.

Physical examination may reveal a contused or lacerated scalp which bleeds but little; skin pale and cool; pupils dilated and possibly fixed; and a pulse which may be slow, rapid and feeble, or imperceptible. Breathing may cease for a short interval, reappearing shallow and with periodic sighing. In all but the severe cases, recovery from this state of collapse commences within a few minutes. Vomiting and straining are common.

Contusion of the brain may be major or minor (32).

In major contusion the patient, instead of progressing towards normal after the effects of concussion have passed off, passes into a state of stupor. He remains stuporous, restless, irritable, drowsy, lies curled up in bed, resents interference, and at night is frequently violent and noisy. The spinal fluid pressure is invariably raised. The first effect of such pressure is to compress the veins giving rise to cerebral anoxemia (stupor and irritability) and if this pressure continues, it leads to compression of the capillaries.

Laceration of the brain. The differential diagnosis between a contusion or a laceration of the brain, and an extradural or subdural hemorrhage may be very difficult. There may be a history

of the "latent interval" although Munro (32) feels that its importance has been overrated. Convulsions are conspicuous by their absence. Physical examination may show some localizing neurological signs, the result of hematoma formation. The unilateral dilatation of the pupils was present in only 50% of Munro's series. Unfortunately, it may be ipsilateral or it may occur on the side opposite the lesion. According to Munro, the neurological signs fail to clear up, unconsciousness deepens, delirium or mania develops, the pulse drops to below sixty, and the cerebro-spinal fluid gets less bloody even though the pressure may be high or low.

Cerebral Vascular Lesions

The diagnosis of acute cerebral vascular insults involves four questions: First, whether the coma is due to a general condition, or a local cerebral cause. Second, the nature of the lesion. Third, its location. And Fourth, a differentiation between the various types of vascular accidents.

The determination of the type of coma (general or local cerebral cause) can be made from the history, physical examination, and laboratory findings. In deep coma, regardless of the cause, all normal reflexes are abolished. But in cerebral lesions, there are generally signs pointing to paralytic involvement of one side of the body. The coma in cerebral hemorrhage and embolism is more or less sudden, while in thrombosis it is slower in onset.

Concerning the history, Solomon and Aring (36) found the following points to be of great value:

1. Sudden onset of coma.
2. Age of patient. More than 90% of their cases were over 40 years of age and 75% were over 50.
3. Previous high blood pressure or heart disease.

E. D. Friedman (20) states that most patients exhibit premonitory symptoms such as dizziness, a sense of pressure in the head hemiparesthesia, anxiety, confusion, disturbances of speech or transitory

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aphasia, loss of interest and ambition, emotional dullness, irritability, tendency to weep, transitory paresthesias, and paralysis; others give a history of high blood pressure, arteriosclerosis, and pathologic urinary changes.

A complete physical examination is essential in all cases since an opinion as to the type of lesion depends more upon the interpretation of a group of corresponding findings rather than upon one or two characteristic signs.

The degree of coma will vary according to the type of lesion and the extent of injury to the brain. Therefore, one cannot rely on this sign in differentiating between the various cerebral vascular lesions.

Complete or partial hemiplegia is almost diagnostic. Solomon and Aring (36) found it present in 57% of their series on entry. Aring and Merritt (3) also found it present in 57% of their series of 245 cases, while six other cases had quadriplegia.

Abnormal pupils were present in about 70% of cases (3). Conjugate deviation of the eyes occurred in about 10% of Aring and Merritt's series, with the deviation towards the lesion in 85%.

"Choked discs" are of significance only in conjunction with the history and laboratory findings. It is usually suggestive of brain tumors.

Stiffness of the neck occurred in 13% of Solomon and Aring's series. This was on entry only. Aring and Merritt reported it present in 62% of their series. The further significance of this sign will be discussed in the differential diagnosis.

Abnormalities in the respiratory rhythm was found in 30% by Solomon and Aring and in 20% by Aring and Merritt. The respiration may

be stertorous, labored, rapid, dyspneic, or of the Cheyne-Stokes rhythm.

Elevation of blood pressure was found in 50% of cases by Solomon and Aring. This compares favorably with the results of Aring and Merritt. Other authors merely mention the "full, bounding pulse" (14) (33).

Temperature changes are not particularly significant. Solomon and Aring reported an increase in 9% and a decrease in 31%. Friedman (20) states that fever usually develops soon after the attack and, if high, is of serious importance. Wechsler (41) states that the temperature usually drops, but a slight rise is not uncommonly observed. According to Aring and Merritt, a practically constant finding in any type of cerebral vascular lesion is the uniform rise of temperature, pulse rate, and respiratory rate several hours or days before death occurs, indicating a collapse of the vasomotor and heat regulating centers.

Aring and Merritt found the "Babinski" toe sign in 50% of their cases in which this test was recorded. It was bilateral in 22%. Solomon and Aring found the sign present only occasionally. Wechsler states that the Babinski sign is generally elicited even in the earliest stages of coma.

Occasionally, the physical findings will show abnormalities of the heart, lungs, eyegrounds, pulse, and Kernig's leg sign.

Convulsions not infrequently occur in cerebral vascular lesions. Aring and Merritt reported the occurrence of convulsions in 10% of their cases while in Solomon and Aring's series, 9% of the patients had convulsions during the examination.

The laboratory tests are invaluable. Out of 78 lumbar punctures, Solomon and Aring found increased pressure in 43 cases, and grossly bloody spinal fluid in 42 cases. Aring and Merritt found increased pressure in 57% of the cases of cerebral hemorrhage and in 22% of the cases of cerebral thrombosis. In their 116 cerebral hemorrhage cases, Aring and Merritt found grossly bloody spinal fluid in 74%, and increased pressure in 57%. In their 106 cerebral thrombosis cases they found only 22% with increased pressure, but rarely, if ever, a grossly bloody spinal fluid.

According to Aring and Merritt, an increase in the blood count over 12,000 was found in 54% of uncomplicated cases of cerebral hemorrhage, and in only 10% of the cerebral thrombosis cases, the counts ranging from 12,000 to 40,000 per cubic millimeter.

The presence of albumin and casts in the urine was found in 60% of 152 specimens reported by Aring and Merritt. Sugar was reported in approximately 10% of the specimens. Solomon and Aring found the urine abnormal in only 11% of their series.

Differential Diagnosis

Cerebral hemorrhage. The history often helps here. A "sudden" onset of coma is more typical of hemorrhage (3) (36) (41) and embolism than it is of thrombosis. The age of the patient, The heart findings, and the course of events will differentiate between hemorrhage and embolism. Abnormalities of the eye are far more frequently found in hemorrhage. Conjugate deviation is twice as frequent in hemorrhage as in thrombosis and, according to Aring and Merritt, unilateral dilatation of the pupils occur in 25% of the case of hemorrhage as compared to only 7% of the cases of thrombosis.

Stiffness of the neck is an extremely valuable sign as indicative of cerebral hemorrhage. Aring and Merritt found it in 55% of their hemorrhage cases, and in only 7% of the cases of thrombosis. The same authors found that convulsions were twice as frequent in hemorrhage as in thrombosis.

A bilateral Babinski reflex was found to be twice as frequent in hemorrhage as in thrombosis (3).

THROMBOTIC OCCLUSION	CEREBRAL HEMORRHAGE
Prodromes frequent	Prodromes infrequent
Great degeneration of the arteries of the limbs, or the history of syphilis	Turged face and strongly beating arteries of the neck
Pulse soft and often very compressible	High arterial tension, regardless of the size of the pulse
Heart feeble, dilated and irregular	Heart hypertrophied and beating strongly
Coma less marked in depth and duration	Coma more intense and longer in duration
Following grief and other depressing influences	More likely to be induced by mental excitement
Local convulsions more frequent	General convulsion more frequent
Slight initial temperature disturbance	Often great initial temperature disturbance
Slight variation of the temperature within a few hours	Often a considerable rise of temperature from 12-24 hours after attack
Secondary inflammatory symptoms frequent and well marked	Secondary inflammatory symptoms less in frequency and in degree

Fig. 6. Points of Differentiation in the Diagnosis of Cerebral Hemorrhage and Thrombosis.

A grossly bloody spinal fluid is indicative of hemorrhage. It was found in 74% of cases of hemorrhage, and rarely, if ever, in thrombosis (3). An increase in pressure was found in 57% of hemorrhage as compared to 22% of the cases of thrombosis.

Cerebral thrombosis. The history is of value here also. According to Wechsler (41), a previous history of headaches and dyssthesias, mental symptoms, possibly repeated lesser attacks, and the slow onset, speak for thrombosis and softening. This is in keeping with the opinions of other writers (3) (12) (14), who also stress the significance of a gradual onset, leading to coma and hemiplegia.

Thrombosis, aside from that occurring in the course of infectious disease, generally arises on the basis of arteriosclerosis and syphilitic endarteritis (41). It is most commonly observed in older persons. Aring and Merritt, in their study of 245 cases of hemorrhage and thrombosis, found that arteriosclerosis, as evidenced by examination of the peripheral vessels and those of the retina, occurs more frequently and is more advanced in cases of cerebral thrombosis.

The colloidal gold curve of the spinal fluid should be mentioned here as having no differential value in the diagnosis of cerebral vascular lesions (3), while a positive blood Wasserman would only complicate the picture and necessitate differentiation between a cerebral vascular accident and syphilis of the central nervous system.

The table in fig. (6), published by Eskeridge in 1898, (14) gives a good summary of the points of value in the differentiation between hemorrhage and thrombosis, and will help the reader to more clearly distinguish between these two types of apoplexy.

Cerebral embolism. According to Wechsler (41), cerebral embolism is more common in young people, occurs in the course of mitral stenosis, in fibrillating hearts, or in subacute bacterial endocarditis; there may be evidence of other emboli elsewhere, especially in the retinal arteries and, unless a very large vessel has been occluded, the coma is not generally deep or of long duration. Other writers (3) (12) (36) mention the extreme "suddenness" in onset, the lessened depth of coma, and the tendency to recover consciousness more rapidly.

Of the five cases of cerebral embolism in Solomon and Aring's series (36), four showed auricular fibrillation and one a severe rheumatic carditis. Aring and Merritt found abnormalities in 94% of their 18 cases of cerebral embolism.

The paralysis is more likely to be defined, the brain substance not being ploughed up as in hemorrhage but a definite area being rendered anemic (41). Aphasia is slightly more frequent with embolism as the common carotid is a more accessible path for the emboli. Alford (2) found that definite and permanent confusion of consciousness was present in 27 out of 55 right sided hemiplegias, while it occurred in only one out of 33 left sided hemiplegias.

Brain Tumor. Aside from the fact that a hemorrhage into a tumor, which has previously been quiescent, may simulate cerebral vascular disease, and be diagnosed correctly only by the subsequent course of events, it is frequently difficult to differentiate between progressive cerebral softening or encephalomalacia and tumor of the brain. This is especially apt to be the case in older persons. Generally, headache is much more severe, "choked disc", by far, more common, vomiting more distressing, and the progress considerably slower in tumor.

Abscess of the brain will only rarely come up for diagnostic differentiation. The previous history of local infection or abscesses elsewhere and the general symptoms are the guiding criteria.

Progressive local atrophies of the brain are generally accompanied by symptoms of senile dementia or presenile psychosis, (Alzheimer's disease), progress much more slowly, and show fewer focal signs than cerebral softening.

The diagnosis of organic from hysterical hemiplegia should offer no difficulties. In hysteria one can nearly always find a psychogenic cause. There is no Babinski, no loss of superficial reflexes, and no abnormal associated movements can be elicited.

Poisoning

A history of attempted suicide is of vast importance. Evidence of the nature of the poison may be present in the form of syringes, medicine bottles, or receptacles. Relatives may volunteer information concerning the taking of drugs such as luminal, amytal, codeine, or bromides. Otherwise it becomes necessary to make a complete physical examination, gastric lavage, etc., in order to determine the particular poison.

Differential Diagnosis

The patient in coma from carbon monoxide poisoning, perhaps, presents the least difficult problem. The depth of the coma is usually light, and there is a strong odor of illuminating gas on their breath. The face often has the characteristic bright "cherry red" color. The temperature is always subnormal and the pulse high. When given a mixture of oxygen and carbon dioxide to breathe, the patient often recovers consciousness quickly. Spectroscopic examination of the blood will give the characteristic

absorption bands of carbon monoxide.

Diagnosis of coma due to poisoning from one of the barbital derivatives presents a difficult problem. In the absence of a history of attempted suicide, or of information volunteered by friends and relatives, diagnosis rests upon testing the gastric contents or waiting until the patient revives, which usually occurs within 24 to 48 hours. In twelve cases, Solomon and Aring found that frequent after effects were blurred speech, nystagmus, tremor of the hands, and absent tendon reflexes. A skin rash rarely occurs.

Bromid Poisoning: History of taking bromides over a long period of time. Blood and special fluid examination will reveal an increased amount of bromides present.

Potassium Permanganate Poisoning: The finding of a purple colored stain on the tongue and in the mouth is of value. The vomitus and stomach washings will reveal the presence of the drug.

Compound solution of Cresol: The characteristic odor of "lysol" on the breath of the patient; in the vomitus and stomach workings, together with burns about the mouth and face should make the diagnosis far from difficult.

Opium Poisoning: The pupils are minutely contracted to the typical "pin point" stage, except just before death, when they may dilate. The breathing is shallow, slow, labored, irregular, and perhaps stertorous. The respiratory rate may be as low as four per minute. The pulse is slow and compressible. The skin is cold and moist, and the features are pallid and cyanotic. The patient finally dies of respiratory paralysis with deepened cyanosis. Vomiting or twitching may occur. The temperature is always subnormal. In some instances, the odor of opium may be detected. Gastric lavage and analysis will verify the tentative diagnosis.

Lead Poisoning: In saturnine encephalopathy the symptoms are rather variable. Convulsions may occur. One should always examine the mouth very carefully for the blue line upon the gums. French () suggests evaporating the urine to dryness and testing for lead in the residue. Lead may also be tested for in the feces. Information concerning the occupation of the patient will help considerably in clearing up the diagnosis. X-ray of the bones, revealing deposits of the heavy metal will verify the diagnosis. Ophthalmoplegias chiefly affect the sixth nerve.

Epilepsy

The diagnosis of epilepsy should not be difficult. The most important information is obtained from the history. The fit consists of

- a. The aura.
- b. The cry, sometimes.
- c. The tonic stage.
- d. The clonic stage.
- e. The comatose stage.

A history of previous attacks confirmed possibly by scars on the head or body should always be significant.

Physical examination will reveal wounds or scars on the tongue. Saliva may be churned up in the mouth. Convulsions often occur during the physical examination. The patient is usually young.

The most characteristic feature of this type of coma is the rapidity with which it disappears, providing the patient is not suffering from an acquired cranial injury. For the first few minutes after the convulsions coma is profound. Then there follows total relaxation and absence of reflexes. Very slowly the patient gets simply sleepy and can easily be aroused. The deep reflexes are then increased. Headache and confusion usually succeed and the mental state of the patient is dull and depressed.

Differential Diagnosis

Cerebral syphilis. Suspect this when the first attack occurs in a middle aged patient who has previously been well and strong. The absence of a typical epileptic history; the failure to find scars on the body or on the tongue; and the positive Wasserman of the blood and spinal fluid serve to clear up the confusion.

Apoplexy. Convulsions in apoplexy are not common, but they do occur. Little difficulty should be encountered here. The age of the patient; the full, hard pulse and increasing blood pressure; the presence of signs of hemiplegia; the progressively deepening coma; the stertorous breathing; and the increase in temperature, all give the clinical picture of anything but epilepsy.

Disseminated Sclerosis. Multiple sclerosis may also give rise to similar attacks and coma, and the age of the patient

may serve to further confuse the diagnostician. Here, again, any information from relatives or friends would be of value in ruling out epilepsy. Absence of scars or wounds on the tongue or body would be against a diagnosis of epilepsy, while the finding of a "paling" of the optic disc would further fortify the possibility of disseminated sclerosis.

Diabetes

The history of a gradual onset is so typical of this type of coma that one may disregard the rarer forms mentioned by Osler wherein coma is ushered in suddenly, following exertion. Usually one obtains a history of diabetes, dietary indiscretions, recent polydipsia, recent respiratory infections, or localized infections such as boils, nausea, vomiting, or epigastric pain. . As pointed out by Solomon , the condition of the pupils are of no value here.

On examination the following signs should be searched for:

Temperature subnormal, in absence of infection.

Kussmoul's "air hunger".

Dehydration.

Acetone odor to the breath.

Soft eyeballs (due to low intro-ocular tension.)

Pulse quick and soft.

Laboratory tests will reveal the presence of sugar and acetone and diacetic acid in the urine; increase blood sugar , and lower inter-spinal pressure. The acet~~o~~uria is not emphasized by many authors as being important, but I feel that in doubtful cases, the presence or absence of acetone in the urine is highly significant in helping to rule out other frequently confusing causes.

Differential Diagnosis:

Cerebral Hemorrhage. As pointed out by Forsythe, some

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diabetics meet death by way of apoplexy and the physician must bear this in mind when making a diagnosis of diabetic coma in elderly patients. Additional symptoms and findings such as the presence of a hemiplegia, a hard slow pulse, and rising blood pressure would point to an accompanying cerebral hemorrhage. A lumbar puncture may disclose increased spinal pressure or a bloody cerebro-spinal fluid. The history of a sudden onset should make one suspicious of some additional factor.

Hyperinsulin shock: In hypoglycemic shock, the more important points which aid in the differentiation are:

The history of a more sudden onset of coma, very often accompanied by convulsions.

The absence of dehydration in most instances.

The absence of "Kussmaul's" air hunger and acetone breath.

The negative urine and the lowered blood sugar.

The differentiation between this and diabetic coma should not prove difficult. Inquire as to whether any insulin has been given before hand and search for syringes and insulin bottles.

Meningitis

Important points in the history are: headache, fever, projectile vomiting, convulsions, stiffening of neck, upper respiratory infections, ear trouble, mental disturbance, chills, diplopia, and paralysis. The three symptoms stressed by most authors in common are those of the headache, projectile vomiting, and stiffening of the neck (12) (36) (41).

On examination one usually finds some of the following clues:

Elevation of the temperature.

Stiffness of the neck and extension of the head.

Positive Kernig's sign and Babinski toe sign.

The youth of the patient. One half of the series seen by Solomon and Aring (36) were under 10 years of age.

A bulging of the fontanelle in infants.

Cranial nerve involvement.

Irregular respirations.

Slow and irregular pulse in presence of increased intracranial pressure.

Evidence of a primary infection in lung.

Symptoms pointing to infection about the head.

Changes in the optic disc. Such changes would be more

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important in indicating a primary tumor or abscess and secondary meningial inflammation. The greater the swelling of the disc, the greater the probability of the primary intracranial lesion being a tumor.

Laboratory examination will show:

1. Spinal fluid is abnormal in every case, being grossly purulent in a large percentage of cases (36). The white blood cells and protein are increased, and the sugar and chlorides are decreased. The causative organism will be found by smear or culture.
2. Urinary findings are not considered as important by the better authorities (18) (36) (41).
3. Roentgen studies of the chest may reveal tuberculosis or pneumonia.
4. Blood culture may be positive in a small number of cases.

Differential Diagnosis

The differentiation between the exciting bacterial causes of meningitis will be determined by smear or culture of the spinal fluid. Aseptic meningitis should be considered when repeated culture and smears are negative for organisms.

Brain Abscess: As a rule the signs are usually focal and a history would reveal symptoms pointing to the temporal lobe (speech and field defects) or to the cerebellum (nystagnus and cerebellar phenomena). In the absence of a reliable history, the negative laboratory findings would decide in favor of brain abscess as against meningitis.

Brain Tumor; Coma from brain tumor is rare and hardly need be confused with meningitis. The most important finding would be the definite "choking" of the optic disc. Incidentally, the laboratory procedures would all decide against a diagnosis of meningitis.

Pneumonia

Pneumonia is not mentioned in textbooks as one of the causes in which coma is a presenting sign. In Solomon and Aring's (36) series, it was as common as diabetes and three times as common as uremia. The majority of cases occurred in the young and very old.

Important points in the history are: cough, fever, sudden pain in the side, chill, abdominal pain, and bloody sputum.

The chief diagnostic physical signs are:

1. Elevation of temperature and increase in pulse rate.
2. Age of the patient.
3. Rapid respiration.
4. Cyanosis.
5. Signs of consolidation.

Blood counts, urinalysis, and lumbar puncture are of no diagnostic value. Blood culture may give positive cultures of the pneumococcus.

Differential Diagnosis

Cardiac Decompensation. The history of sudden loss of consciousness and previous heart disease in an elderly patient should serve as a valuable clue. The physical findings of abnormal heart, dyspnea, pulmonary congestion, peripheral edema, ascites, enlarged liver, and cyanosis should decide the diagnosis. Further evidence of cardiac pathology will be revealed by examination.

Cardiac Decompensation

A previous history of heart disease or high blood pressure is important. The age of the patient should always be considered since cardiac decompensation occurs chiefly in individuals over sixty years of age and usually with a sudden onset.

The chief diagnostic physical signs are:

1. Cardiac abnormalities.
2. Cyanosis.
3. Temperature normal or slightly increased.
4. Signs of pulmonary congestion.

5. Peripheral edema.
6. Dyspnea.
7. Enlargement of the liver.

Laboratory tests are of no value as a rule. Blood and urine analysis may be normal or abnormal. Roentgen examination may or may not reveal an enlarged heart.

Differential Diagnosis

Apoplexy. A history of previous "strokes" or high blood pressure; the suddenness of onset, and the neurological findings indicate cerebral hemorrhage. The absence of cyanosis or signs of congestion, and cardiac abnormalities decide against cardiac decompensation. An increase in blood pressure under observation would serve to verify a "stroke".

Syncope. In transient coma from simple fainting the symptoms are fleeting in character and pass away on return of proper cerebral circulation.

Syphilis of the Central Nervous System

The diagnosis may be made in every instance by laboratory procedure alone, but may be tentatively made easily if a few principles be kept in mind. As pointed out by Sprigg (37) in 1904, cerebral syphilis should be suspected when unexplained convulsions occur in middle aged patient who was previously well and strong. Any history of previous syphilis, with treatment, should arouse suspicion. The coma, severe though it may be, tends to pass off rapidly in a way that would not be the case had it been a hemorrhage of corresponding severity.

The important physical signs are neurologic: convulsions, abnormal pupils, the Babinski sign, and oftentimes other abnormal reflexes, depending upon the depth of the coma. Paralysis is usually absent, but when present, only serves to confuse the original diagnosis of central nervous system lues.

Laboratory work is most important, but requires time before the report is ready. The blood and spinal fluid Wassermans are usually positive, and the colloidal gold test may reveal a "paretic" curve in many instances. The Kline and Kahn tests may be performed quicker.

Differential Diagnosis

Cerebral Hemorrhage. This may occur with or without convulsions in middle-aged adults, but the absence of other signs such as profound and deepening coma, signs of hemiplegia, thickened arteries, rising blood pressure, rapid appearance of fever and respiratory paralysis, and blood in the spinal fluid together with a negative Wasserman test should differentiate a "stroke" from central nervous system lues.

Cerebral Thrombosis. This is more gradual in onset and local rather than generalized convulsions are present if at all. The coma is deeper and does not tend to pass off rapidly. The physical findings of hemiplegia and negative blood and spinal fluid Wassermans will favor a thrombosis.

Epilepsy. The history of previous convulsive attacks, the youth of the patient, the scarred tongue, and the accompanying "aura" differentiate epileptic coma from that due to syphilis.

Meningitis. The history of previous vomiting and headache; the presence of stiff neck and retracted head; positive Kernig and Babinski reflexes, together with a grossly purulent spinal fluid should offer no difficulty in diagnosis.

Eclampsia. The physical findings of pregnancy, the high blood pressure, evidence of kidney damage, and the negative blood and spinal fluid Wasserman, could hardly be confused with a convulsion due to central nervous system lues.

Uremia

A history of previous kidney trouble, high blood pressure, headache, vomiting, dyspnea, convulsions, or recent infections is

especially pathognomonic of uremic coma. According to Spriggs (37), the most characteristic feature of the convulsions is the fact that they are repeated, alternating with coma, being either typically epileptic or merely muscular twitchings, and may come on suddenly. Friedman (20) states, however, that the onset of coma in uremia is gradual, preceded by headache, vomiting, and evidence of intoxication.

The helpful physical signs are muscular twitchings, acetone on the breath, abnormal eyegrounds, enlarged heart, increased blood pressure, edema of the extremities, Cheyne-Stokes respiration, and the peculiar anemic or yellow tinged skin.

Important laboratory changes are gross abnormalities of the urine and increased non-protein nitrogen of the blood. If lumbar puncture be done the non protein nitrogen will be very high.

Differential Diagnosis.

Cerebral hemorrhage. The normal or slightly elevated non-protein nitrogen of the blood; the typically sudden onset of coma; the age of the patient; the history of previous stroke, or high blood pressure; the physical findings of thickened or beaded arteries, signs of hemiplegia, rising blood pressure, and Hutchinson's pupil favor hemorrhage.

Forsythe (18) warns us that when uremic coma affects a hemiplegic distribution, it may succeed in passing itself off as a unilateral lesion, most probably a hemorrhage, and that, whatever the explanation may be, this much must not be forgotten: "that uremia, at one time or another, simulates most cerebral conditions."

Epilepsy. The youth of the patient, the history of previous "fits", the clonic muscular contractions, the scarred or bitten tongue, and the rapidity with which the coma disappears, favor epilepsy. The absence of abnormalities of the urine, and the normal non-protein nitrogen

of the blood verify the diagnosis.

Coma due to eclampsia.

A history of pregnancy is practically always obtained(36). Other important points in the history would be headache, increase in blood pressure, edema, albuminuria, vomiting, and convulsions. The patient is, of course, in the child bearing age,(up to 45 years).

The diagnostic physical signs are: abdominal tumor, convulsions, edema of the extremities, high blood pressure, and rapid pulse. Solomon and Aring (36) found a rapid pulse in every one of their seven cases.

Laboratory findings will reveal an abnormal urine in every case(36).

Differential Diagnosis

In an epileptic, the signs of toxemia are absent and the coma will pass off more rapidly. The urine will be within fairly normal limits. The history will further verify a diagnosis of epilepsy.

Alcoholism may produce convulsions in a pregnant woman, but here, as in other instances, the typical findings of an eclamptic seizure, with coma, are absent,- edema, elevation of blood pressure and rapid pulse. Alcohol may produce a marked albuminuria, but this will disappear as the effect of the intoxication wears off. The alcoholic odor of the breath must not be confused with acetone. The patient recovers as the effect of the alcohol disappears.

COMA ROUTINE

In favorable cases the physician may be fortunate enough to obtain a history of events preceeding the onset of coma, which, undoubtedly greatly helps to make a quicker and more accurate diagnosis. In most instances, however, the reverse situation is present and the doctor is thrown upon his own resources in making a search for the underlying cause. Consequently, the ability to observe, interpret, and evaluate the clinical signs and manifestations of recognized value, should be a part of the observer's general knowledge if he is to logically and scientifically proceed along a definite path in searching for the cause or causes producing the state of unconsciousness in his patient.

A coma routine, whatever may be the order of procedure, as long as it includes a thorough evaluation of all items of importance that need be considered, is most desirable for speed and accuracy of diagnosis.

Such a routine represents a systematic approach to the confronting problem. It not only saves precious minutes and hours of time, but it prevents many embarrassing attempts to explain overlooked clues in wrongly diagnosed cases that should have been diagnosed correctly had a definite routine

proceedure been followed "to the letter". Many an overlooked skull fracture with rupture of the middle meningeal artery could have been interpreted correctly had the patient been given the advantage of roentgen ray study when signs of trauma or compression were suspected.

Forsythe, in 1912, (18) advocated a form of proceedure which he adopted for the study of a patient in coma. He first estimated the depth of coma by the patient's response to stimuli. Next, a comparison of the muscular tone of both sides was made, followed by auscultation of the heart, paying special attention to the pulse and respiration. For the rest:

"if his tendon jerks are feebler on one side than on the other, or his pupils unlike in size and mobility, or if, being alike, they are very small or very large, or if his tongue goes to one side or his temperature rises--these observations will sum up most of what can profitably be learned from the examination."

Regarding special investigations, Forsythe favored four:

1. Analysis of the urine for albumin and sugar.
2. Inspection of the retinae for albuminuric retinitis, optic neurites, or specific choroiditis.
3. Lumbar puncture, with examination of cerebrospinal fluid.
4. Analysis of stomach contents for poisons.

He practically always carried out the first two tests, reserving the last two only for particular cases. It is interesting to note that more recent articles (5)(20) include lumbar puncture with detailed spinal fluid examination as a

part of their coma routines.

To again quote Forsythe:

"The kernel of the whole subject, however, is group I. Here, as a first step in the differential diagnosis, it is useful, as a rule, to separate on the one hand: cerebral hemorrhage, thrombosis, embolism, and injury, from, on the other hand: epilepsy, uremia, diabetes, poisons and Adams-Stokes disease; or broadly speaking, the unilateral lesions from the bilateral lesions. "

Herbert French, in 1917, (21) followed a general but by no means specific, coma routine. He fails to mention the importance of laboratory tests or other special procedure such as blood, urine, or spinal fluid examinations.

Briefly stated, French carried out the following procedure:

He attempted to get the most out of any information presented in the history. Then he examined the patient, looking first for any evidence of unilateral paralysis: unequal pupils, one cheek puffed out more than the other, a limp arm or leg, differences in the knee jerks or plantar reflexes, or conjugate deviation of the eyes. In the face of distinct evidence of unilateral paralysis, he concluded that there was almost certainly a cranial or intracranial lesion: hemorrhage, embolism, fracture, tumor, abscess, thrombosis, or meningitis. Next, he examined the head with particular care to see if there were any signs of injury, remembering that the patient may have had a cerebral hemorrhage with coma, in which case the injury was due to the

coma, and not the coma to the injury. He mentions the difficulties which may arise on this account, particularly when the patient had previously imbibed of alcohol sufficient to cause an alcoholic odor on the breath, and to suggest that the patient was drunk. The careful observation of the patient for several hours was necessary as an aid in settling the diagnosis. He also examined the ears and nose with care to determine whether cerebrospinal fluid or blood was coming from either, as an indication that there was a fracture of the base of the skull. Blood coming forward into the subconjunctival tissue was interpreted as affording similar evidence.

Bishop and Applebaum, in 1929, (5) devoted an entire article in presenting a simple and practical coma routine. It is, by far, the most complete, though brief, summary of a coma routine published, to date. The dire need for a practical method was aptly stated when the authors said,

"For some time we have felt that unless a systematic routine is followed in the investigation some very important items may be overlooked. We believe that the following coma routine is simple and practical."

A brief resume' of Bishop and Applebaum's coma routine is as follows:

I. History. They emphasize the importance of as detailed a history as possible, getting additional information from visitors who come in later.

II. Physical examination. Special attention is paid

to the head, eyes, and ears. A complete neurological survey is also made. The blood pressure is taken immediately and repeated at definite intervals.

III. Laboratory studies include the following items.

1. Urine. A catheterized specimen is obtained on admission and sent to the laboratory for study.
2. Spinal fluid. A complete study is made, including: appearance, amount, pressure, cytology, smear, culture, albumin, globulin, and sugar. Wasserman and colloidal gold where indicated.
3. Blood examination. Red and white count when indicated. Blood chemistry is given special preference, especially for non-protein nitrogen and sugar. Wasserman when indicated.
4. Gastric analysis. A careful study of the stomach contents is very important in their opinion, especially where there is a question of some form of poisoning.
5. X-ray of the skull. The authors found this to be a most necessary step, especially in the diagnosis of suspected fracture of the skull.

They conclude by stating:

"We believe, that by following a definite routine in coma, we can more often arrive at a correct diagnosis. There is room for a more careful survey of various aspects of coma and we are following the routine for a time and hope to be able to make some valuable tabulations."

Friedman, in 1933, (20) presented a rather well written paper concerning the care of coma from unknown cause. He emphasizes the importance of the history, physical examination and laboratory work, much the same as did Bishop and Applebaum, and also gives a more detailed discussion of the important items to consider in the history and physical examination.

Any further attempt to formulate a coma routine would, necessarily, be a repetition of much that has already been written. A more detailed outline would be very convenient, especially in the form of a printed page or questionnaire with spaces provided for the information gathered from each case. Repeated experiences with coma cases would automatically reduce the problem to a mechanical procedure and the internist would be able to conduct the routine without the aid of the printed outline. Such a plan would be both practical and valuable for any large hospital where many patients are admitted in coma each year. The writer will probably publish, at a future date, a more complete and detailed outline of a "coma routine" designed for the use of admitting internes who are frequently confronted with the problem of diagnosing the cause of coma as a presenting sign.

CONCLUSION

In conclusion the writer might state that he was impressed by the undesirable but conspicuous diversity of opinion throughout the literature regarding the differential diagnosis of coma. This was especially true of the earlier writers. The more recent articles on this fascinating subject are few as yet, but are ever so much more in harmony, and will, undoubtedly, continue as such, as the mysteries of "coma" are unravelled.

By choosing a subject of this nature, in spite of its vast scope, the writer feels that he has benefited greatly both by the knowledge gleaned, and by the experience gained in searching through the literature. It is hoped that the material collected in the various chapters will be of value to those who seek to gain more information concerning the differential diagnosis of coma as a presenting sign.

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