DELIRIUM AND RELATED PROBLEMS

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DELIRIUM AND RELATED PROBLEMS

The Golden Bough, by Sir James Frazier, began as a study of the rule of succession to the priesthood at Ariccia in the Alban Hills of Italy. However, to understand this, Frazier was required to continually examine larger questions, until he ended with twelve volumes and a comprehensive theory of primitive religion. At one time, an article about delirium might have been simple; all that would have been required was to catalogue the myriad syndromes that affect the brain, as though the severity of the central nervous system insult explained all. But the story turns out to be a good deal more complicated than that. The investigation of the multitude of factors actually responsible for delirium production has raised general and profound questions concerning the nature of brain function, the mechanisms of sleep and dreams, the importance of man's environment, the interaction of mind and body, and the mode of action of licit and illicit drugs. Delirium is the psychosomatic syndrome par excellence, a final pathway of often coexistent physical and psychological disturbance. Yet, as recently as 1967, Lipowski lamented that delirium was the "Cinderella of English-language psychiatry: taken for granted, ignored and not considered worthy of study." New developments in brain physiology, the advent of Rapid Eye Movement technology (REM) allowing new insight into sleep and dreaming, research into sensory deprivation and overstimulation, the model psychoses of hallucinogenic drugs, the development of medical-surgical techniques causing

delirium, e.g., open-heart surgery, or preventing it, e.g., renal dialysis, have all combined to cause considerably more interest in this increasingly complex subject. Ten years ago it was simpler; intensive care units (ICU) could be built without windows since patients would be unconscious or semiconscious and not need them. It is now recognized that of all the facilities of a general hospital, the ICU and recovery rooms need windows the most.

There used to be a saying that to understand syphilis was to understand all of medicine. To understand delirium fully requires us to understand fully the patient's world: physical, environmental, social, and intrapsychic. The concept of multidetermination is as applicable to delirium as to symptom or dream formation. We will begin by looking at the syndrome in general terms, and then turn to the specific situations in the general hospital where delirium is most likely to occur.

History

Delirium is such a ubiquitous phenomenon that it was well known to the ancient world. The Greeks and Romans clearly identified an acute reversible brain syndrome distinguishable from chronic mental illness, and called it "phrenitis" or "phrensy." Fever was a common cause, and Hippocrates noted visual hallucinations and picking at bed sheets. Plato and Aristotle noted the similarity of dreams to the visions of the mentally ill. Celsus saw the relationship between mind and body, realizing that delirium was caused by debilitating systemic illness, and was a serious prognostic sign auguring death. Delirium tremens was described by Aretaeus and Galen and in the fifth century by Cassius Felix.

The Talmud, compiled in the first five hundred years a.d., describes a reversible syndrome of "Kordiakos," attributed to drinking new wine from a vat. When convulsions were described, light wine was prescribed for therapy, and this might very well also have been related to delirium tremens.

Delirium was of course known to poets and writers before it attracted the attention of modern scientists. As has been noted, Shakespeare eloquently describes Falstaff's final illness in *Henry V.* "For often I saw him fumble with the sheets and play with flowers and smile upon his fingers' ends, I knew there was but one way, for his nose was sharp as a pen, and a'babbled of green fields." (II, iii). He also recognized the role of psychological stress, "The

king has kill'd his heart." (II, i).

In the modern era, Thomas Willis's conceptualization has been summarized by Lipowski. Wilson realized that delirium could be produced by infection, intoxication, malnutrition, and visceral disorders. Postsurgical delirium was described by Pare in the sixteenth century, and investigated by Dupuytren in 1819. The nineteenth century witnessed great interest in the phenomenon of hallucinations, as schizophrenia was delineated, and the effect of hashish studied.

Freud's contribution to the theory of delirium has not received sufficient notice. In the *Interpretation of Dreams,* he pointed out that the content of deliria is partly related to the individual's experience; "even the deliria of confusional states may have a meaning . . . they are unintelligible to us owing to the gaps in them." In the essay on Leonardo da Vinci, he pointed out the similar mechanisms of dreaming and hallucinations; "a phantasy . . . must have *some* meaning in the same way as any other psychical creation: a dream, a vision or a delirium." In this connection he quotes Radestock: "Both in patients suffering from fever and in dreamers, memories arise from the remote past, both sleeping and sick men recollect things which waking and healthy men seem to have forgotten." Freud also saw the working of the mental apparatus, and that even in delirious states the unconscious never overcomes the resistance of consciousness "so that the secret of the

childhood experiences is not betrayed even in the most confused delirium."

As Lipowski has noted, the German psychiatrist Bonhoeffer classified deliria, noting that specific etiologies could produce many types of delirium reactions. Nonetheless there remained great terminological confusion, partly relieved by the authoritative work of Engel and Romano. Delirium was conceptualized as a syndrome of cerebral insufficiency, that could be monitored by following the slowing of the electroencephalogram (EEG). Hyperactivity, hallucinations, or agitation were not necessary for the diagnosis. Delirium was defined as any acute, reversible syndrome of cerebral insufficiency. Lipowski has introduced the concept of delirium as a *psychosomatic condition,* in which both physical and psychological factors interact causally. Psychological factors, such as sensory input, sleep deprivation, the stress, setting and care of the medical illness, all were seen as possible precipitating or intensifying factors in delirium etiology.

Classification

A number of related terms are used with different meaning to different people. *Delirium,* which dynamically and historically should include all acute brain syndromes, is used by many people to refer only to agitated hallucinating patients. *Confusion, metabolic encephalopathy, acute brain syndrome,* and *psychosis associated with organic brain syndrome* are, conversely, sometimes applied only to the apathetic confused patient. The issue is further complicated by the suggestion that the terms hyper- and hypoactive delirium be used to make that distinction. However, this overlooks the shifting and protean nature of the symptoms of delirium in any given patient. These distinctions are quantitative, not qualitative. Delirium represents a broad syndrome of disturbances in sensation, perception, memory, thought, and judgment. It can run the gamut from a slight reduction in alertness to coma, and indeed patients may pass through this sequence in both directions, as their disease waxes and wanes.

In its mildest form it resembles alcohol intoxication, or hypnagogic or hypnopompic phenomena, particularly in a strange place. It begins with a mild clouding of perceptions, with a subjective lack of focus, blurring or haziness. It is only with an effort that thought processes can be channeled into logical and coherent patterns. Memory, especially for recent events, becomes impaired. Speech and thinking become slowed, and the right answer

is obtained with delay. Perplexity, uncertainty, and vagueness are communicated as the patient looks around searching for an answer. With partial preservation of cerebral functioning, there may be moments of insight into the perceptual, thought, and memory disturbances. Symbolic and abstract thinking dwindle. Time disturbance appears with inability to give the day of the week, hour of the day, or date. Place disorientation may occur, with the hospital identified as home or as a branch of the hospital close to home. Grasp, retention, and the capacity for attention are impaired. Patients become distracted and fail to distinguish the relevant from the irrelevant. Conversation becomes limited, with a tendency to short monosyllabic phrases. Thought becomes disordered and fragmented with perseveration, and an ultimate poverty of ideas. Drowsiness follows in many patients, while others are restless and unable to sleep. Affect can be shallow or, in more labile forms, irritation and agitation appear, with hypersensitivity to light and noise. Headache may be present.

In the fully developed syndrome, the clouded sensorium and disorientation proceed, and thinking may be so disconnected as to produce incoherent speech. No matter how great the effort, reading becomes impossible, and so may conversation. Progressive loss of motor control appears with drooling, food spilling, poor food intake and hygiene, and unkemptness. Ultimately, incontinence of urine and feces occur. This may occur initially in dreams with ensuing shame, but in the end even the social

excretory conventions may be lost. Lack of contact with the environment may be extreme, with total time and place disorientation and misidentification of family members. Motor signs such as tremor, slurred speech, seizures, increased autonomic activity appear, with fever, sweating, injected conjunctivae, flushed countenance, rapid pulse, pilomotor responses, and diarrhea. Patients may sleep only during the day when sensory cues are sufficient to reorient and lessen anxiety, but night combines anxiety with reduced sensory input, preventing sleep.

The fully developed syndrome is not merely the worsening of the mild form but contains novel elements of the greatest scientific interest. It is the appearance of hallucinations, initially reported as dreams, that raise major questions. As Lipowski has noted, there is difficulty in estimating their frequency, with a range of 39-73 percent. Visual hallucinations are generally the most prominent, although the auditory modality is frequently involved, and authors have commonly observed proprioceptive hallucinations in postcardiotomy and tank respirator patients. Hallucinations are less marked in the aged and in chronic disease. Lipowksi has raised three critical questions with regard to the hallucinations: Why do they occur at all? Why are they largely visual? How are they shaped by the ego's conflicts?

West has provided a framework for answering these questions. His analogy conveys the reciprocal relationship between reality and illusion . . . "a

man in his study standing at a closed glass window opposite the fireplace, looking out at his garden in the sunset. He is absorbed by the view of the outside world. He does not visualize the interior of the room in which he stands. As it becomes darker outside, however, images of the objects in the room behind him can be seen reflected dimly in the window glass. For a time he may see either the garden (if he gazes into the distance) or the reflection of the room's interior (if he focuses on the glass a few inches from his face). Night falls, but the fire still burns brightly in the fireplace and illuminates the room. The watcher now sees in the glass a vivid reflection of the interior of the room behind him, which appears to be outside the window. This illusion becomes dimmer as the fire dies down, and finally, when it is dark both outside and within, nothing more is seen. If the fire flares up from time to time, the visions in the glass reappear." For West, "perceptual release" explains both the hallucinations of the delirious and the sleeper's dream. For both to occur, there must be a decrease in strength of the inhibiting forces controlling release of recorded precepts, along with sufficient preservation of arousal to permit the discharge of perception-bearing circuits. With relative sensory deprivation during sleep, as well as in sensory restriction experiments, and perhaps in delirium, residual awareness no longer competes with current awareness, and the perceptual traces are released and re-experienced, sometimes in rearranged form. This would also explain the effect of sensory overload which "jams the circuits." In sleep, environmental

awareness diminishes, yet the cortex is functioning sufficiently to allow for discharge of memory, altered by the censorship of the weakened sleeping ego. Optimal conditions for hallucinations (or hallucinogens) would be disturbed sensory input while maintaining or enhancing arousal. Similarly, sub-hallucinogenic drug doses in the presence of sleep deprivation may also produce hallucinations.

By inference, it would appear that delirious hallucinations are primarily visual, for the same reason that dreams are. It is likely there is a greater amount of visual memory, of unusual intensity. It seems less likely that nonspecific visual stimuli, produced within the visual pathway's anatomy provides the raw material, awaiting only secondary elaboration.

The visual hallucinations themselves vary widely in duration, vividness, complexity, and relationship to other modalities. Particularly vivid, intense hallucinations are seen in withdrawal syndromes, and we have also seen them in postcardiotomy delirium.

Course

The course of delirium is characterized by fluctuation and variation, often in the presence of apparently constant organic findings. In many instances, this may be due to variations in emotional and environmental factors, although unrecognized physiological changes in brain metabolism may also occur.

Symptoms may last from moments to weeks, but rarely longer than a month. Postcardiotomy delirium generally lasts several days. In the series by Morse et al. on postoperative delirium over half of the patients recovered within a week, and three-quarters eventually recovered completely. Termination can also be by death or by passing into a chronic dementia. Together with Frank, we have shown the absence of permanent organic deficits in patients with the postcardiotomy syndrome. Obviously the likelihood of persistent organic deficiencies are dependent on the nature of the physical factors contributing to the delirium.

During the acute phase, with the savage physical assault on brain function, various release phenomena appear. Unchecked id or sadistic superego are no longer counterbalanced. Lack of inhibition, or depression and paranoia can emerge. Once again, the more acute the syndrome, the more disruptive it is to the defensive apparatus, and more primitive defenses appear. Given overwhelming catastrophe there is a great tendency to blame

the self or others. In *Risk,* the author hallucinates that the surgeon has operated on her to "get a brilliant article." A frequent delusion is that the staff is out to kill the patient, which is also a projection of the rage felt for being forced to endure pain and suffering.

Obviously, the premorbid personality determines the quality of release phenomena. Obsessive-compulsive personalities with emphasis on performance may be hit hard by their inability to meet self-set standards, and be terrified by weakly opposed aggressive and sexual impulses. Soiling may produce extreme humiliation. Active personalities may react with outward blame and heightened vigilance. For each patient, the unique blend of premorbid personality, organic insult and clinical setting will shape the content and even appearance of delirium.

Examination of the Delirious Patient

The skilled interviewer can often detect reduction in the level of cognition during a routine history. Woven into such an interview can be questions about dates of onset, admission, length of time in the hospital, vital statistics etc., so that considerable information can be gained without exposing the patient to a humiliating quiz in which he knows few of the answers. The exposure of deficits may hinder further cooperation and foster antagonistic attitudes. Arithmetic calculations are often used in less obvious cases. The use of serial sevens and repetition of digits backward has been scored by Katz et al. It has value in obtaining sequential state measures, but fails in deliria characterized by relatively clear cognition, but with perceptual aberrations or place disorientation. In severe cases, the month and year may provide an easily obtainable barometer. In answering questions, the delirious patient may not only make errors, but may respond slowly, utilize concrete aids, like his fingers, or try to conceal his deficit by attacking the question.

Differential Diagnosis

Delirium must be suspected in any behavioral or emotional problem in a patient who is seriously ill or exposed to sensory or movement restriction. Dementia or chronic organic brain syndrome is usually ruled out by a history of long-standing intellectual deficit, along with a relative absence of agitation, affect, and hallucinations. However, dementia may only be diagnosed when the underlying acute precipitant is treated and cognitive deficits persist. Quite common is the worsening of a mild dementia by an acute organic illness or stress to create a delirium, just as the added insult of sodium amytal may precipitate severe confusion in a mildly organic patient.

At the other extreme, delirium must be distinguished from purely functional illness. The EEG can often answer such a dilemma. Intravenous sodium amytal, judiciously given, can also be helpful in the differential diagnosis since the patient with delirium will get worse. In a patient with a functional disorder, this etiology will become more apparent. This test should be given with great care in situations where the patient's physical condition can be compromised by its use. Most difficult is the clinical differentiation between retarded delirium and retarded depression. The depressed patient may complain of memory loss related to his lack of interest, difficulty in concentrating, and need for self-abuse. However, the mental status should reveal the absence of confusion. The hallucinating schizophrenic tends to be

younger and have primarily auditory hallucinations. Once again, the sensorium will be clear. Dissociative patients tend to not know who they are, a great rarity in delirium. They generally also have a model for their symptoms, a history of previous hysterical symptomatology, and are in a stressful situation to which the delirium-like symptom is a compromise solution.

Incidence

As Reding and Daniel have pointed out, delirium is frequently missed because of inadequate mental status examination, failure to notice nurses' notes, difficulties in distinguishing between normal aging and pathology, and insufficient use of the EEG. They also cite an overemphasis on psychodynamics. There is no doubt that nonpsychiatrists often miss the diagnosis. Stated most baldly by Hoaken, "On surgical wards . . . the last thing of interest . . . is the patient's general behavior and mental state." In view of these problems of diagnosis, the true incidence of delirium can only be estimated. Select groups, such as cardiac surgery patients, have a high incidence, and the presence of large numbers of such patients can skew a sample. Nonetheless, Skoog reported a 15 percent incidence in patients admitted to a Swedish hospital. As in certain other studies, women had a greater susceptibility. Foreigners were particularly vulnerable probably because of lack of social and linguistic contact. In 1938, Cobb and McDermott made the same observation of a high incidence in foreigners, some of whom lacked obvious physical explanations. Even then, they suggested loneliness and strangeness as possibly causal factors. Lipowski, in reviewing the German literature, cites the estimate of Bleuler et al. that 30 percent of the 20-70 year old population will, within their lifetime, sustain an episode of delirium, and that 5-10 percent of medical patients in a general hospital suffer from it. The rate is clearly higher for patients over sixty years, where it may approach 50

percent. One estimate is that one-sixth of psychiatric consultations in the general hospital are requested for organic brain syndrome.

Brain Pathophysiology

Although toxic factors are not the whole story of delirium, consistent brain pathophysiological problems have been demonstrated in metabolic encephalopathies. The brain's problems in oxidative metabolism can be replicated at altitudes over 12,000 ft. and at blood sugar levels below 60 mg. percent. Posner has summarized the pertinent neurophysiology. For reasons that are not well understood, cerebral oxygen uptake declines in proportion to the severity of the metabolic brain disease. The normal brain receives 55 ml. of blood per minute, about 15 percent of the resting cardiac output. If the flow falls, more oxygen and glucose are initially extracted. But if the oxygen tension of cerebral tissues falls below 4 mm. Hg, unconsciousness is inevitable. There is no cerebral storage of oxygen and within only six seconds of deprivation, coma occurs. A four-minute interruption of oxygen supply almost always causes irreversible damage, and after fifteen minutes virtually all nerve cells are dead. The brain is less demanding for glucose, its only physiological substrate. One hundred g. of brain utilizes 5.5 mg. glucose per minute, 85 percent of which reacts with oxygen. There is a reserve of 2 g. of glucose to allow 90 minutes of metabolism without irreversible damage.

In addition, the brain requires enzymes and cofactors (vitamins and electrolytes) to function. It is believed that metabolic derangements such as vitamin deficiency, electrolyte imbalance, and exogenous and endogenous

poisons operate by inhibition of the cofactors. Nonetheless, the precise mechanism of uremic and hepatic coma, two of the most common metabolic poisonings, are not even known. Although diminished oxygen uptake is a biochemical common denominator, there is no proven anatomic one. Moreover, there is even disagreement as to which area of the brain is most vulnerable to metabolic insult. The traditional view was that the most primitive neural structures were best preserved, and the most recent phylogenetic acquisitions least protected. In this sequence, the cortex is affected initially, then subcortical structures. Pathological studies of anoxia and hypoglycemia support this view, as do animal studies where cortical electrical activity disappears first. A more recent theory holds that the brain stem reticular formation is most vulnerable and that cortical neurons stop functioning when no longer stimulated from below. In some animal studies, electrical transmission through the reticular formation ceases while the cortical neurons are still able to receive other afferent input. Clinically, it would seem that the cortex is first attacked as decline in cortical function preceded alteration of consciousness. Posner concludes that regional issues such as energy needs, blood supply, etc., may determine the point of maximum vulnerability.

Electroencephalographic Findings

The normal EEG has an 8-13 cycle per second (cps) base frequency. The degree of slowing from this baseline parallels the degree of dysfunction. In metabolic disease bilateral synchronous bursts of 1-3 cps are superimposed on a 5-7 cps background. This slowing is an extremely consistent finding, and monitoring it allows for an accurate reading of the clinical state. Slowing parallels worsening and acceleration improvement. Change is more important than absolute values; an initially high-frequency alpha may fall into a normal range with delirium. The EEG is not specific to any single etiology, but is affected by the intensity and duration of the metabolic problem. Recent advances in computer technology have allowed the study of evoked responses. Anticholinergic drug-induced delirium has been associated with abolition of visual response after rhythm, resembling those of sleep. Itil found anticholinergic hallucinogens to produce EEG's with a marked increase of slow waves with superimposed high-frequency fast activity. Fast beta waves were related to an increase in hallucinations. Studies of the EEG during REM sleep may shed further light on the electrical manifestations of image formation.

Of great theoretical significance is the discovery that sensory restriction can produce EEG changes. This material has been summarized by Schultz. Heron was able to show progressive slowing of the EEG and

dysynchronization of the alpha rhythm persisting for hours after a sensory restriction experiment. There were noticeable EEG changes during hallucinatory periods. Zubek et al. found less alpha activity during hallucinations, as well as an excess of theta activity especially over the temporal lobes. Later he demonstrated a mean decrease in occipital lobe frequency, albeit a highly variable one. This variability may be related to differential susceptibility to sensory restriction. Moreover, Zubek and Wilgosh showed occipital lobe slowing following immobilization in a coffin-like box without sensory restriction. In this connection, it was also shown that the EEG slowing due to sensory restriction could be diminished if exercise was permitted. Immobilization alone could also produce intellectual and perceptual impairments.

Metabolic Disturbances in Delirium

All diseases that can disturb the brain's homeostasis can produce delirium. There is little specificity to any etiologic agent. Specificity would have to be associated with a selective rather than general effect on the brain. Sedative or alcohol withdrawal syndromes which produce extreme agitation and florid hallucinations may be such an instance. The intensity is also related to their acute onset, while chronic debilitating illness leads to a quieter syndrome. It should be borne in mind that organic factors often coexist with one another in producing delirium, and that their effect is modified by psychological and environmental factors. An outline of the protean types of disorders that can contribute to delirium is given in the following list.

Organic Causal Factors in Delirium

I. Intrinsic central nervous system (CNS) disease

A. Tumor

1) Primary

2) Secondary

A. Infections

1) Encephalitis

2) Abscess

3) Meningitis

4) Neurosyphilis

5) Fungal and protozoan

B. Epilepsy

C. Ischemic

1) Diffuse or multifocal blood vessel obstruction

2) Large-vessel disease

a) Thrombosis

b) Embolism

3) Intravascular coagulation

a) Collagen disease

b) SBE (subacute bacterial endocarditis)

D. Hypertensive encephalopathy

E. CNS bleeding

1) Subarachnoid

2) Subdural hematoma

3) Bleeding diathesis

a) Purpura

b) Clotting disturbance

c) Leukemia

F. Degenerative

1) Senile

2) Presenile

3) Metabolic errors

4) Demyelinating

II. Non-CNS vascular disorders

A. Hypoxia due to pulmonary disease

B. Hypoxia due to cardiac disease

1) Congestive heart failure

2) Arrhythmia including cardiac arrest and Stokes-Adams

3) Shock as with myocardial infarction

4) Valvular disease as with aortic stenosis

C. Reduced peripheral resistance

D. Disorders of blood volume and viscosity

1) Polycythemia

2) Cryo- and macroglobulimemia

E. Anemias and hemoglobinopathies

1) Pernicious anemia

2) Carbon monoxide

3) Methemoglobinemia

III. Non-CNS organic disease

A. Liver

B. Kidney

C. Lung

IV. Endocrine hypo- or hyperfunction

A. Thyroid-myxedema, thyrotoxicosis

B. Parathyroid: hypo- and hyperfunction

C. Adrenal: Addison's and Cushing's, pheochromocytoma

D. Pancreas: diabetes, hypoglycemia

E. Pituitary hypofunction

V. Ionic or Acid-base Imbalance

A. Water intoxication or dehydration

B. Hyper- and hyponatremia

C. Hyper- and hypokalemia

D. Hyper- and hypocalcemia

E. Hyper- and hypomagnesomia

F. Acidosis, metabolic or respiratory

VI. Infections

A. Acute, such as: pneumonia, typhoid, malaria, acute rheumatic fever

B. Chronic

VII. Environment

A. Low-oxygen hypoxia

B. Starvation hypoglycemia

C. Vitamin deficiencies: thiamin, niacin, pyridoxine, B_{12}, folic acid

D. Heat and electricity

E. Radiation

VIII. Exogenous Poisons

A. Medications

1) Sedatives, barbiturates, and other hypnotics

2) Minor tranquilizers: diazepam, chlordiazepoxide

3) Phenothiazines

4) Opiates

5) Anticholinergics

6) Tricyclic antidepressants

7) Alcohol

8) Anticonvulsants

9) Digitalis

10) Quinidine

11) Salicylates

12) L-Dopa

13) Penicillin

14) Steroids

B. Poisons

1) Methyl alcohol

2) Ethylene glycol

3) Organic solvents

4) Heavy metals

5) Organophosphorus insecticides

IX. Withdrawal syndromes

A. Alcohol

B. Sedatives and hypnotics

In tropical countries, special emphasis must be placed on trypanosomiasis and malaria as causes of delirium. They may produce either gross or localized disturbances in the sensorium or seemingly functional syndromes. Trypanosomiasis, with its insidious course, may particularly lead to loss of interest in work, avoidance of friends, and cyclothymia, before

proceeding to confusion, lethargy, and somnolence. Falciparum malaria infections produce a more acute syndrome. Parasitized red cells with greater adhesiveness and reduced deformability block central nervous system capillaries, until the lumens are obliterated by vast numbers of parasites (Figure 2-1). Characteristic changes can then be seen in anoxic neurons (Figure 2-2). Later changes, with peripheral hemorrhage, including necrosis, demyelination, and gliosis are shown in Figure 2-3). There is a danger, however, that an erroneous causal connection is made when malarial parasites are found in the blood of a delirious patient. Other causes of delirium must be excluded.

It should be underscored that failure to recognize and treat the physical causes of acute delirium may result in permanent brain damage. Unrecognized, and hence untreated myxedema and pernicious anemia are particularly tragic examples of this. The diagnosis of pernicious anemia may be especially difficult when folic acid treatment prevents the characteristic hematological picture from emerging, also emphasizing the lack of correlation between the anemia itself and cerebral symptoms. The latter may be produced by endarteritis leading to anoxia (Figure 2-4) and accompanied by demyelination (Figure 2-5)

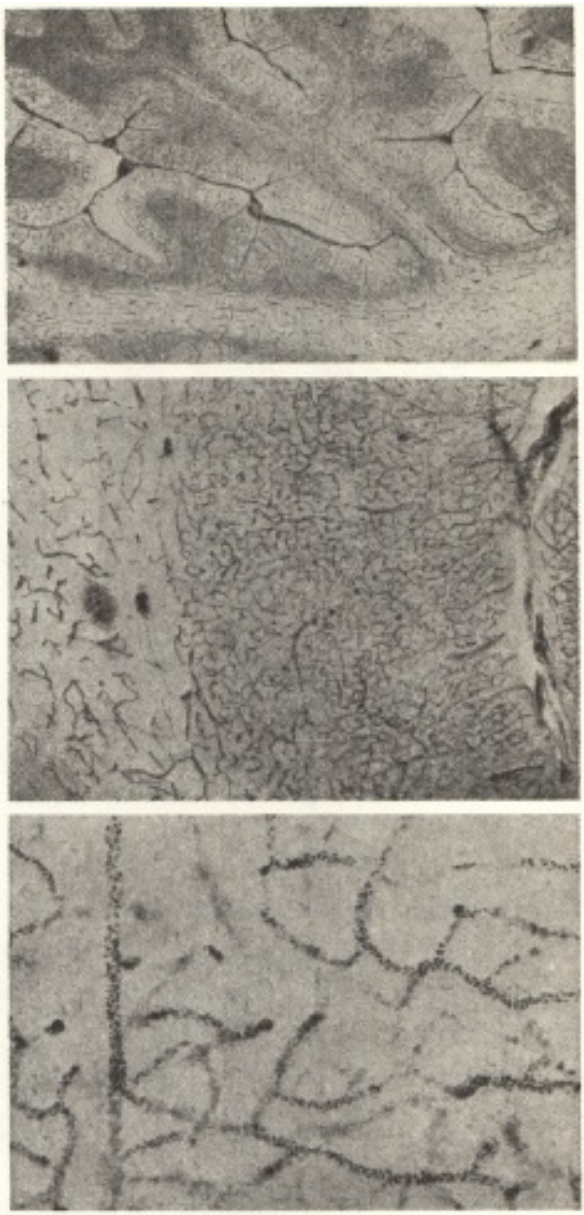

Figure 2-1.

(top) Case of cerebral malaria due to *Plasmodium falciparum*. Photomicrographs from unstained frozen sections, 120 to 200 microns thick. The malarial pigment, which is contained in the vessels, outlines the vascular pattern. Cerebellar angioarchitecture (low magnification), (center) Section from a cerebral area (low magnification), showing the difference in the vascular pattern in the cortex (right part of the picture) and in the white matter (left part). In the white matter it is possible to recognize a small hemorrhagic area, represented by a group of extravasated dots of pigment, (bottom) Section from a cortical area (medium magnification), revealing that the coloration is due to the granules of malarial pigment contained in the capillaries. (Courtesy of Dr. Silvano Arieti and the Archives of Neurology and Psychiatry.)

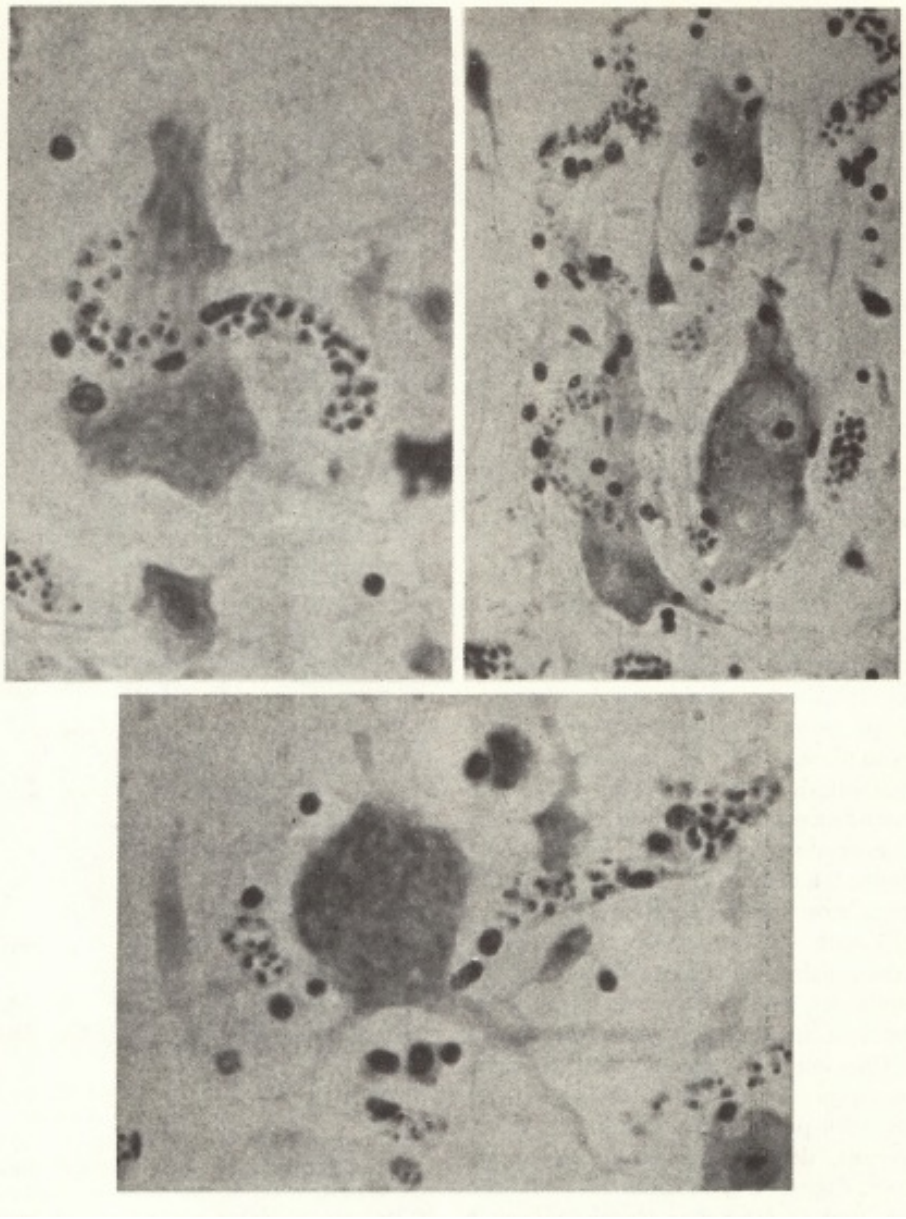

Figure 2-2 .

(upper left) Case of cerebral malaria due to *Plasmodium falciparum*. Betz's cell, surrounded by a capillary loaded with parasites. Notice the dissolution of tigroid substance in the cytoplasm of the nerve cell, (upper right) Betz's cells, showing retrograde (axonal) degeneration. The nucleus is displaced, and the tigroid substance is dissolved in the center of the cell but preserved at the periphery. Notice, also, the large number of parasites in the neighboring capillaries, (bottom) Ganglion cell of the motor area, showing acute swelling. Nissl stain, high magnification. (Courtesy of Dr. Silvano Arieti and the Archives of Neurology and Psychiatry.)

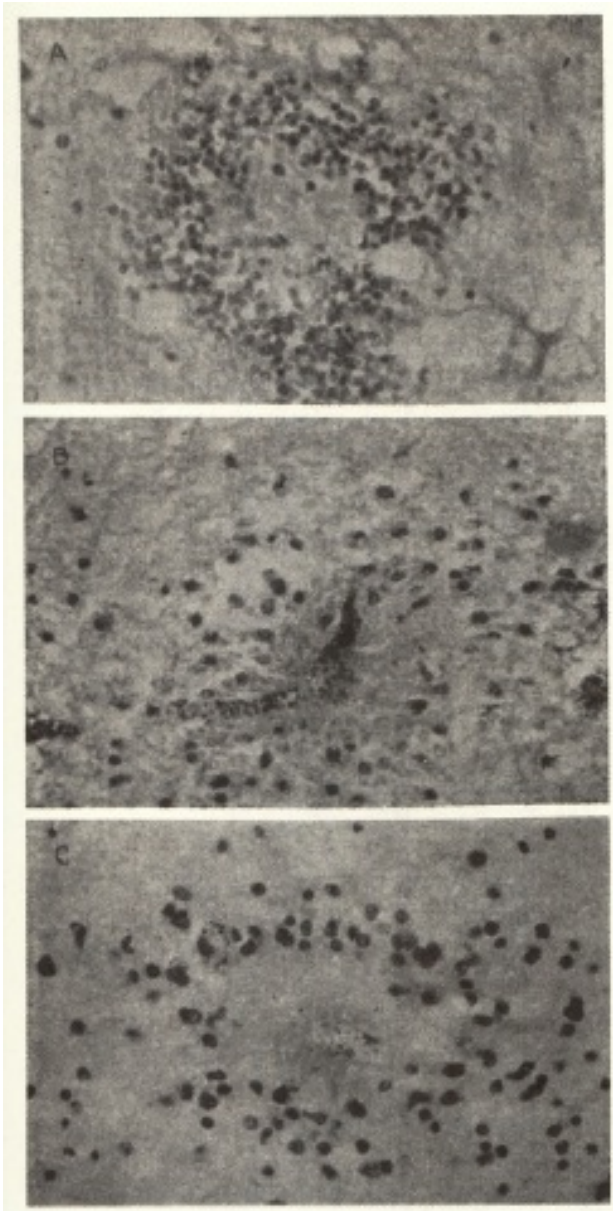
A
B
C

Figure 2-3.

(top) Case of cerebral malaria due to *Plasmodium falciparum*. Formation of a pseudogranuloma. In a small subcortical hemorrhage, the red cells have almost completely disappeared from the center of the area (only a few are left in radial positions) but are still numerous at the periphery. Mallory stain, medium magnification, (center) The red cells have disappeared from the peripheral area also. This area appears edematous and of loose consistency and shows proliferation of glial cells. Note also a central capillary loaded with parasites. Giemsa stain, medium magnification, (bottom) The Pseudogranuloma is now almost formed. At the center one sees in cross section a capillary loaded with parasites. A necrotic central area is surrounded by a peripheral cuffing consisting predominantly of glial cells. Nissl stain, medium magnification. (Courtesy of Dr. Silvano Arieti and the Archives of Neurology and Psychiatry.)

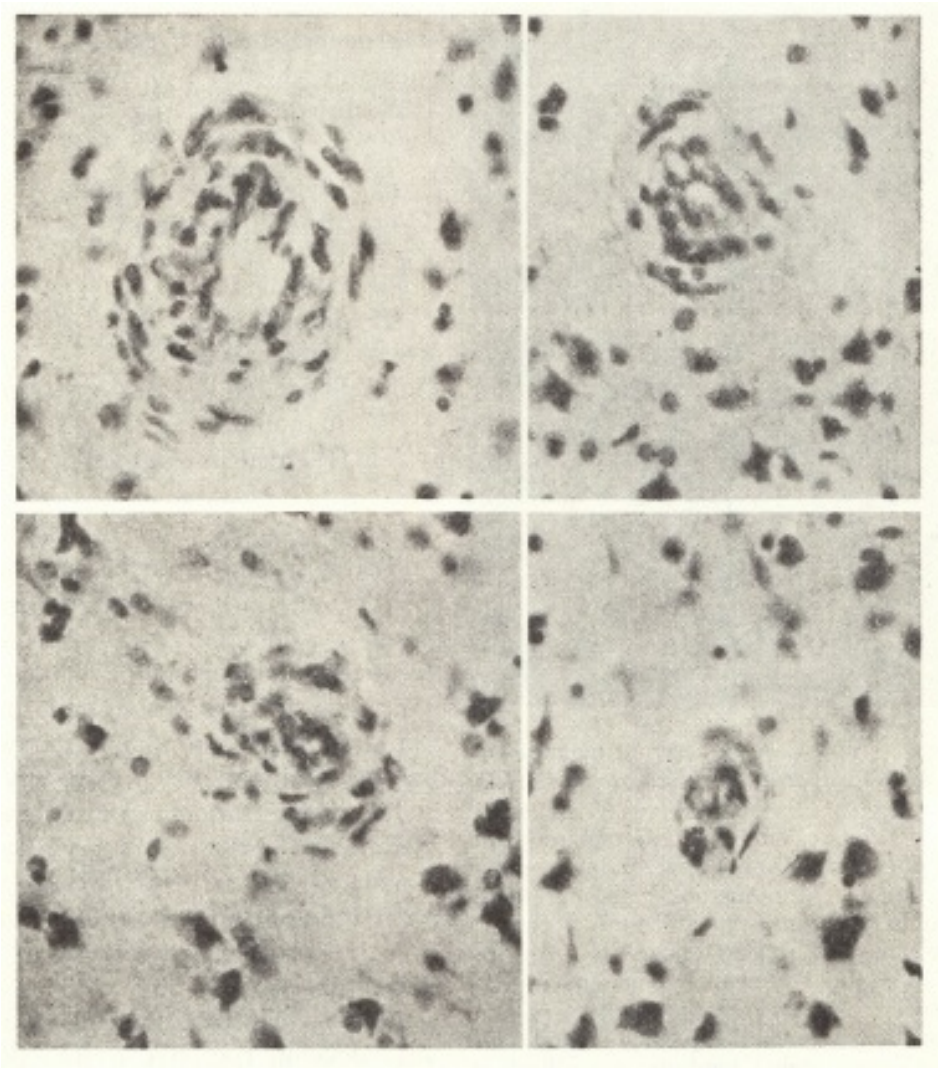

Figure 2-4.

(upper left) Progressive stages of endoarteritis in brain of patient suffering from

psychosis accompanying pernicious anemia. Vascular walls moderately thickened, (lower left) More advanced stage. Vascular lumen conspicuously reduced, (upper right) The lumen of the vessel is considerably narrowed. Recanalization has already taken place, (lower right) Cortical capillary, the lumen of which is completely occluded. Nissl stain. (Courtesy of Drs. Armando Ferraro, Silvano Arieti, and W. H. English and the *Journal of Neuropathology and Experimental Neurology.)*

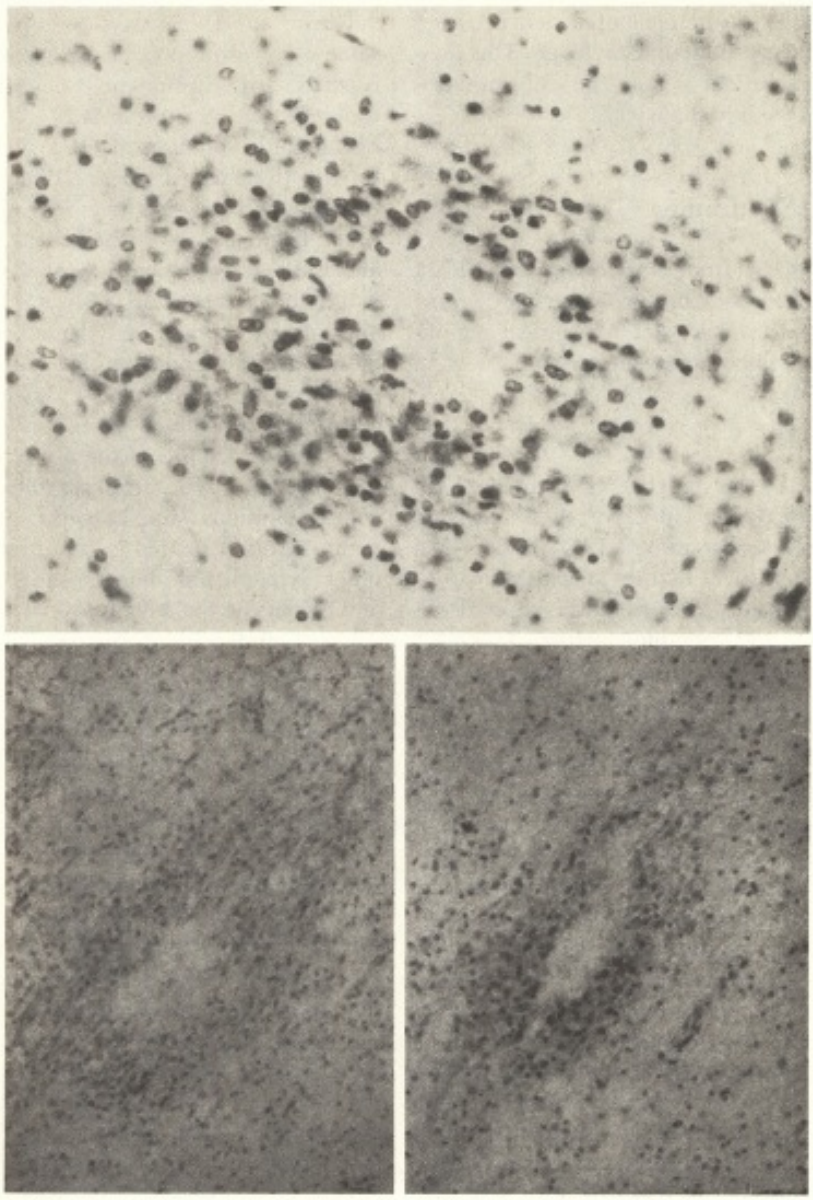

Figure 2-5.

(top) Case of psychosis accompanying pernicious anemia. Nissl stain. Typical Lichtheim's plaque consisting of a central degenerated area surrounded by a crown of glial nuclei, (lower left) Plaque showing two acellular areas, (lower right) Plaque showing an elongated acellular area which probably follows the coruse of a vessel. (Courtesy of Drs. Armando Ferraro, Silvano Arieti, and W. H. English and the *Journal of Neuropathology and Experimental Neurology.)*

Roads to Hallucinations and Cognitive Dysfunction

The general hospital provides natural experiments in which the following conditions, that can cause delirium, are combined.

Causes of Perceptual and Cognitive Impairment

I. Organic insult

II. Sensory monotony

III. Sensory overload

IV. Sleep and dream deprivation

V. Immobilization

VI. Overwhelming anxiety

Sensory deprivation is believed to be responsible for the hallucinations of sailors, explorers, and perhaps even religious figures. Numerous studies have demonstrated the frequent development of hallucinations, impairment of time sense, and impaired perceptual-motor performance following sensory monotony. It is most effective when combined with immobilization, as in total-immersion experiments. Similarly, sensory bombardment via immersion in a geodesic dome with psychedelic light and sound can also produce cognitive impairment, particularly in field-dependent subjects.

Subjects deprived of sleeping and dreaming also develop cognitive dysfunction, at times with hallucinations. Hallucinations of a purely functional nature arise when massive anxiety requires the use of primitive mechanisms of denial and projection. In this regard, Arieti's concept of the expectant attitude is relevant. The paranoid listens to the environment expecting to hear his own critical self-appraisal.

As we shall see, there are situations in the general hospital highly conducive to delirium production. Each of them will be examined in turn. However, virtually all patients are subjected to some of the etiologic factors. A physical disease is invariably present. Patients are separated from their familiar environment, family, and even their clothes, and placed in single rooms fostering monotony, or in busy wards leading to overstimulation. Hearing aids or glasses are misplaced or removed for fear of loss. The same may also be true of television sets and radios. Physical symptoms or the strange environment may interfere with sleep. Sedatives that can cloud consciousness are prescribed for sleep or tranquilization and given in larger doses if not initially successful. Anxiety is rampant and suspiciousness regarding medical care is always possible. Margolis, has focused on the violations of patient's privacy in the ICU. Processions of doctors, nurses, aides, volunteers, equipment mechanics, floor scrubbers, relatives, and friends may troop through. They see the patient at his worst, his weakness exposed.

In the laboratory, subdelirium levels of one factor combined with subdelirium levels of another can produce delirium. Safer duplicated West's finding with anticholinergic hallucinogens and sleep deprivation. Half of a hallucinogenic dose of scopolamine plus one sleepless night was equivalent to a full hallucinogenic dose.

In 1936, while investigating the delirium associated with a course of five to ten hyperthermia treatments, Ebaugh et al. discovered that 43 percent of delirium patients had only a single episode, 80 percent of which occurred during the first induction of fever. The inescapable conclusion is that the delirium was fostered by the initial anxiety.

Special Syndromes

A number of syndromes are associated with a high incidence of delirium. Since they are of great theoretical, as well as clinical significance, they will be examined in detail.

Eye Surgery

With the former practice of patching both eyes after cataract surgery, sudden visual deprivation was imposed. This produced a delirium referred to as the "black patch psychosis" which illustrates the interaction of environmental and organic factors. Jackson has reviewed the extensive literature in this area over the last eighty years.

Cataract patients tend to be old and already suffering from some chronic brain impairment. Retinal detachment patients are younger, but have a more acute illness and greater restriction of postoperative movement. Both groups have high levels of anxiety about the possibility of blindness. Colman in 1894, first reported postoperative hallucinations. In 1900, Posey reported twenty-four cases of delirium in elderly patients with patched eyes. "The delirium began with mental restlessness and rapidly progressed to hallucinations and ideas of persecution. Delirium developed during the second day for eight patients; the third day for six; and the fourth day for two." This delayed response supports the idea that the restriction operates

gradually to contribute to the delirium. Moreover, the eye surgery, done under local anesthesia, does not provide a fresh organic insult to the brain. In 1913 Parker reviewed the charts of a large series of cataract extractions. Patients were described as "restless, maniacal, suspicious, uncontrollable, and disoriented; getting out of bed; talking incoherently and removing their patches" (maybe not so unwisely!). Once again the delirium began after a latent interval from one to six days postoperatively, the same range as in most postsurgical delirium. A report in 1917 by Brownell described the syndrome as lasting a day or two.

Our understanding of etiology is enhanced by the dramatic discovery that, despite the covering of both eyes, the delirium was more apt to begin and/or worsen at night. Weisman and Hackett eloquently wrote ". . . night . . . is the time when a hush falls on the ward, and auditory cues, which may have been responsible for alerting and orienting the patient during the day are replaced by silence with an occasional whispered conversation and the soft sporadic sounds of the night. Under these circumstances . . . misinterpretations may become delusions and anxiety may become panic." Added to this is the mystique of the night symbolizing danger and vulnerability, and increasing the anxiety.

Coles and Linn suggest trial patching prior to surgery if it is absolutely required. Delirium could be predicted when the EEG was abnormal and the

sodium amytal test positive. In high-risk patients, surgical techniques may have to be modified, keeping in mind the patient's likelihood of noncooperation. Early mobilization and stimulation of the patient, as might be obtained in a two- to four-bed room, were recommended. Ziskind et al reported the highest delirium incidence in the non-English speaking, the deaf, alcoholics, or those with obvious brain damage. Jackson noted the great variability in insight, and that patches were most frequently removed by patients at night. It seems clear that bilateral patching should be avoided and that removal of patches may have dramatic therapeutic effects.

Respirator Delirium

The phenomena of respirator-induced delirium was described by Holland and Coles in 1955 following an outbreak of poliomyelitis. Forty percent of bulbar polio patients developed delirium beginning from one to ten days after entering the respirator. Hallucinations and delusions were of a pleasurable nature, frequently involving motion and travel. The emotional stress was enormous. Patients feared that they would be unable to summon help, since they could not close their tracheotomies should there be a power failure or the plug be pulled accidentally. They faced the prospect of possibly permanent paralysis or even death. As time in the tank progressed, patients became depressed, finally showing hostility and anxiety with weaning from the respirator. Disorientation and confusion were also noticed.

Mendelsohn and Foley provide an explanation of this syndrome. The hallucinations occurred in a quasi-twilight state. They disappeared when the patients' limbs were manipulated or when someone spoke to them about their real surroundings. They could not see their bodies, their vision was restricted, hearing was impaired due to the repetitious motor sound, and mobility was restricted by the paralysis and tank confinement.

Extending their clinical observations, seventeen normal control subjects were put in the respirator. Only five could remain in it longer than thirty-six hours. Eight sustained hallucinations and all were unable to concentrate or judge time. Four had to terminate abruptly due to severe anxiety. Moreover, the subjects were not febrile, and they knew they could get out, walk, and breathe at any time.

Mendelsohn et al. structurally analyzed the hallucinations. In general, hallucinations are wish-fulfilling or defensive. The latter tend to be auditory, the former multisensory. They are facilitated by great anxiety and need in schizophrenia, or in the nonschizophrenic subjected to enormous stress. The polio patients' hallucinations had both wish-fulfilling and defensive characteristics. Movement motifs were enhanced by the vibration of the pump motor. Hallucinations were extremely colorful, three dimensional, and generally pleasant. They served the wish of being able to move again, yet reality intruded to the extent that tank-type structures followed them along

as they anticipated their future lives.

The tank-respirator syndrome is now observed in patients with chronic lung disease, such as kyphoscoliosis. It is also seen in neurological diseases, especially if they combine paralysis with decreased sensation. Intermittent removal from the tank, if possible, is recommended.

Cardiac Surgery

In 1964, Blachly, Egerton and Kornfeld et al. described a syndrome occurring in the open heart recovery room (OHRR), three to five days postoperatively. Logically, it was named postcardiotomy delirium. It often began with illusions based on sounds created by the machinery in the room, and with frequent proprioceptive distortions such as a rocking or floating sensation. Patients would become briefly, or persistently, disoriented. Delusions were common, sometimes with a frank paranoid flavor. One patient thought a record player had been placed under her bed to torture her. She also hallucinated the voices of absent family members. Like most patients, she improved after transfer from the OHRR. Thirty-eight percent of Kornfeld patients were adjudged delirious by chart review, and fully seventy percent of those followed throughout the surgical experience had delirium symptoms. Kornfeld confirmed Blachly's finding that degree of preoperative illness predisposed to delirium. Also confirmed was Blachly's finding of a higher

incidence in double-valve replacement cases, and an association between prolonged cardiopulmonary bypass time and delirium.

Kornfeld reasoned that the lucid interval of several days postoperatively suggested that postoperative factors played a role in delirium causation. Similarities were noted between the OHRR experience and sleep and sensory deprivation studies. It was postulated that the intense anxiety the cardiac surgery patient experienced might also play a part.

A number of recommendations were made to lessen delirium incidence and severity. Uninterrupted sleep was to be encouraged. Individual rooms were suggested to minimize patients waking each other or witnessing anxiety-provoking emergencies. Less obtrusive monitoring equipment was advocated to minimize sensory monotony and anxiety. Increased mobility with early removal of wires and tubes was recommended. The monotonous noise of oxygen, cooling, and air-conditioning apparatus was to be minimized. Television sets, radios, clocks, and calendars were to be supplied to increase stimuli and provide reality cueing.

A more detailed longitudinal study reported in 197030 of 142 survivors showed a decrease in delirium incidence since the early report. Now only 24 percent experienced the delirium after a lucid interval, while 9 percent had evidence of an organic mental syndrome upon awakening from anesthesia.

These latter patients were hypoactive and tended to lack florid symptomatology. They tended to have severe organic illnesses.

The lucid interval delirium group was intensively studied. Organic factors clearly played a role, since advanced age, and severity of pre- and postoperative illness, and time on the cardiopulmonary bypass were all correlated significantly with delirium.

An effort was made in the 1970s to understand the reduced incidence. Decreased bypass time appeared to play a role, as within each operative category reduction in incidence paralleled the varying reduction in bypass time. It was also postulated that the adopted suggestions with regard to sleep and environment, and the less panicky attitude of patients and staff might also be responsible. Other investigators confirmed the role of social-environmental factors in delirium incidence. Lazarus and Hagens studied two groups undergoing open-heart surgery by the same surgeon at different hospitals. In one hospital, modifications designed to lessen anxiety, sensory monotony, and sleep deprivation halved the incidence of delirium. Layne and Yudofsky reported that patients who did not express preoperative anxiety had double the incidence of delirium of anxiety expressors. It seems clear that pre- and postoperative emotional ventilation would play a prophylactic role. This view was further confirmed when a member of our research team reviewed the charts of patients seen by the research group and a comparable

group that had not been seen. The interviewed group had half the delirium incidence of the unseen group.

The present authors have undertaken a detailed study of the personality and psychological factors associated with postcardiotomy delirium. Organic factors were once again found to be significantly related. A new finding, based on statistically significant psychological test reports and suggestive psychiatric ratings, was that patients characterized by dominance, aggressivity, confidence, and an active orientation seemed more vulnerable to delirium. It was reasoned that for such individuals, the passive, immobilized patient role in the OHRR would be more stressful than it would be for more passive patients. For the active group, the OHRR experience is an exact opposite to their usual functioning and produces intense conflicts. Denying anxiety, this group would be unable to benefit from preoperative psychological ventilation which might reduce postoperative anger and paranoia.

All these factors, it should be emphasized, complement rather than conflict with organic risk factors. Other investigators have presented new evidence confirming the importance of organic factors. Tufo has shown that operative hypotension is associated with postoperative organicity. Kimball has emphasized the significance of previous central nervous system insult. Willner et al. have found organically based disturbance of analogy reasoning

predictive of delirium.

Our work has shown a high incidence of delirium, approaching 40 percent, in patients undergoing saphenous vein coronary artery bypass surgery. This is believed to be related to relatively lengthy bypass times and possibly the active-dominant character of the sample. These patients often manifest the time urgency and aggressivity characteristically associated with early onset of coronary disease.

General Surgery

The most straightforward study suggesting that psychological factors play a role in general surgical delirium comes from two small hospitals in El Dorado, Arkansas. The two hospitals have the same bed capacity and medical staff, and accept random admissions. One of the ICUs is windowless, the other has windows. Controlled factors were age, type of procedure, and postoperative temperature. There were no differences between the two groups. Yet the windowless ICU had a 40 percent delirium incidence as compared with 18 percent in the windowed unit. Although it can be argued that there is an unidentified causal difference, it would seem that a room without windows during the critical immediate postoperative period is deleterious.

Comprehensive information concerning general surgical delirium is

found in the work of Morse et al. Probably related to the excellent medical and surgical care at the Mayo Clinic, the overall operative delirium rate was only 0.5 percent. Sixty delirious patients, equally divided between retarded and hyperactive forms were compared with a control group, matched for type of operation, age, and sex. Twenty-two percent of the delirium group had open-heart surgery, 18 percent hip or other fractures, 12 percent spinal fusion, 10 percent colectomy; the remainder had miscellaneous surgery. Delirium occurred from the third to the seventh day postoperatively. Delusions were found in two-thirds of the cases. As would be expected, 55 percent of the delirium patients were over sixty. Age over sixty and duration over one week were bad prognostic signs for recovery.

Abundant support was obtained for the general theory that organic, social-environmental, and emotional factors combine to cause delirium. To be sure, organic physical factors were extremely important. All parameters studied were more likely to be abnormal in the delirium group, and the following significantly so: abnormal EKG (electrocardiogram), albuminuria, alkalosis, anemia, azotemia, hypochloremia, hypokalemia, hyponatremia, and leukocytosis. The delirium group had significantly more cardiac failure, cardiovascular disease, infection, drug or alcohol intoxication or withdrawal, history of organic brain syndrome, preoperative disorientation, operative procedure longer than four hours, emergency operation, postoperative complications, and use of more than five drugs postoperatively. It should be

noted, however, that the abnormalities were not confined to the delirium group.

Yet nonorganic factors also correlated significantly with delirium. Morbid preoperative expectation was associated with a 33 percent delirium incidence as compared with 3 percent not showing pessimism. Sensory distortion, caused by visual disorders or partial deafness, was also much more common in the delirium group, as was a history of more than two previous operations. Denial of preoperative fear was associated with a lower incidence of delirium.

Other, purely psychiatric factors were also significantly correlated with delirium: a history of alcoholism or depression, a family history of psychosis, functional GI (gastrointestinal) disturbance, insomnia, paranoid personality or psychosis, history of previous postoperative psychosis, history of psychiatric treatment, or retirement problems. Patients of the highest social class seemed less susceptible to delirium. Clinical vignettes also supported the psychobiological thesis. In one case, delirium cleared when a misplaced hearing aid was found; in another, it worsened with a son's departure.

Renal Disease

With the development of hemodialysis and transplantation surgery, there has been a renewal of interest in the previously largely academic

question of neuropsychological disorders in end-stage renal failure. Untreated, the mental changes show gradual onset and hence tend to less dramatic manifestations. The usual sequence of events for chronic delirium is followed. Difficulty in concentration and memory change appear associated initially with normal or minimally changed EEG's. This may long precede the development of azotemia. Prodromal symptoms are followed by irritability, labile affect, manifest disorientation and confusion, with delusions and hallucinations. With the neurotoxic crumbling of the personality, dietary indiscretions increase, creating a vicious cycle. Periods of lucidity decline and torpor is common as myoclonus and fasciculations, asterixis and convulsions develop. Lassitude passes into stupor and then coma, usually with heightened muscle tone. Any improvement occurs in reverse order to the loss.

EEG changes parallel the clinical disorder, with slowing usually accompanying BUN (blood urea nitrogen) levels over 60 mg. percent. Initially there is slight slowing with a tendency to disorganization of alpha activity, followed by progressive slowing and disorganization with paroxysms of greater slowness, leading to diffuse slowing and spiking. Tyler claims that the EEG is similar, but not identical to those of hepatic decompensation. Kiley and Hines noted that wave frequency becomes slower before obvious electrolyte changes. Some photic driving, as in a drug withdrawal syndrome, is seen particularly during recovery phases, raising the provocative question of a withdrawal syndrome to an unidentified toxin. Of course, no single electrolyte

correlates with EEG abnormalities, but rapid shifts in electrolytes cause worsening of the EEG and the clinical state. Klinger reports photogenic abnormal occipital sharp waves and Lossky-Nekhorocheff et al. showed disappearance of the alpha rhythm and disturbance of the arresting reaction. Complete records of abnormal slow waves preceded imminent death. Eighty percent of irrational confused patients had abnormally slow frequencies, and if 40 percent of the record is abnormally slow, psychological testing would show cognitive impairment. It should be noted that frequently coexisting diseases, such as anemia and hypertension, can also affect the EEG. Yet the EEG can be used as an indicator for dialysis when there is slowing to less than 6 cps.

But is the treatment any better than the disease? The life of a dialysis patient is dominated by conflicts about the value of staying alive. In the series by Foster, Cohn et al. almost 50 percent of the dialysis patients made suicidal threats. Interestingly, three of the four patients who made attempts succumbed to their disease. Survival was related to physical factors, such as low mean BUN, but also to Catholicism, the presence of parents, and indifference to the fate of other dialysis patients.

Abram has greatly expanded our knowledge of the inner life of the chronic dialysis patient. He classifies the uremic syndrome into the following categories: asthenic, restless, hallucinating, schizophreniform, depressed,

manic, and paranoid. The asthenic category predominates. In a series of thirty-eight patients, psychological testing revealed evidence of organicity in all, with poor visual-motor coordination, and difficulty in nonverbal abstraction and attention. Few patients had acute hyperactive episodes, and when they did occur it was usually during the first episode of uremia, as in the hyperthermia study, again suggesting multifactorial causation.

The initial adjustment to dialysis is euphoria as toxic apathy clears. Anxiety appears at about the third to fifth dialyses, followed by depression as the problems of the treatment become undeniable. Conflicts about dependency and independence emerge and psychotherapy is frequently indicated. From the third to the twelfth month the issue of whether life is worth living becomes paramount. Viederman has well described these problems. The patient has surrendered his autonomy, his clothes are removed, privacy is denied, intake and elimination become subject to the orders of others. There is no dietary freedom. Pain and exposure are experienced two or three times a week for five to eight hours a day tied to a machine. The dialysis bath comes to symbolize the womb and birth, and a love-hate relationship develops with the machine. It becomes the frustrating bad mother, breaking down frequently with ruptured coils and causing weakness, cramps, and hypotension. Such experiences resonate with early maternal encounters. The content of a delirium will clearly reflect this. One of Viederman's patients had the delusion she had been cured by God, and no

longer needed dialysis. Another had the somatic delusion of bodily disintegration with holes in the skin.

According to Abram, life with the machine preoccupies the patient. He becomes a compulsive gambler knowing the only roulette wheel in town is rigged against him, but unable to stop using it. He fantasies or threatens to cut his shunt, the weakest link, the umbilical cord to the machine. He frequently imagines himself a Frankenstein and in his drawings sees himself as increasingly resembling a dialyzer. He has become a semiartificial man, a zombie, the living dead. In fantasy or delusion, mechanical monsters with malevolent intent are after him. Even the nurses dream of the ubiquitous machine and of being dialyzed. They develop psychosomatic illnesses and there is a rapid staff turnover.

Intense relationships develop between patients and staff in this setting. Male patients seeing themselves as castrated may exhibit themselves to the nurses. Particularly where transplantation is considered, patients have great difficulty in expressing anger to the staff for fear of being labelled noncooperative and excluded from the hoped-for miracle surgery. In addition, intense conflicts are experienced concerning family members who do or do not offer their kidneys, and over assuming the identity of the donor. Therefore, both the precipitation and content of any delirious episode must be viewed in the widest possible context.

Hepatic Coma

The delirium associated with liver disease is in many ways similar to that of uremia. In both, we witness a final chapter in a long process resulting in a complex metabolic poisoning. Delirium in liver disease can be divided into two groups, that of hepatic failure, and of portal shunting to the systemic circulation.

The treatment of liver failure, despite the recent use of L-Dopa, leaves much to be desired. There is no hepatic dialysis and symptoms tend to be progressive. A prodromal syndrome is followed by impending coma, often with asterixis (liver flap), and with characteristic, if not specific, EEG findings. There are paroxysms of bilaterally symmetrical high-voltage delta waves 1½—3 cps, along with relatively normal alpha waves.

Organic brain syndromes in patients with liver disease need not be hepatic coma. Delirium can also be caused by anoxia from anemia following gastrointestinal bleeding; central nervous system bleeding caused by a clotting diathesis or head trauma, especially in the alcoholic; inadequately metabolized sedatives or tranquilizers; and the effects of alcohol or its withdrawal.

The differentiation between delirium tremens (DT) and hepatic coma is particularly important since sedative-replacement therapy can be lethal for

the impending hepatic coma patient. The DT's patient will characteristically have abstained from alcohol one to three days before the appearance of symptoms, be more alert, aggressive, and have more vivid hallucinations. His tremor will be coarse and rhythmic. The chronic liver-disease patient, on the other hand, is hypoactive, tends not to have intense hallucinations, and has an irregular and flapping tremor.

Portal-systemic encephalopathy is the term applied to delirium caused by portal shunting, which may be congenital or surgically acquired. It can be produced with or without accompanying liver disease. Clinically it is similar to impending hepatic coma, although at times there may be unique elements. It has a chronic course with recurrent episodes of stupor or coma. Patients may also manifest other neurological signs and symptoms as the illness progresses. These may become irreversible. These patients can mistakenly be thought to be taking excessive quantities of sedatives or tranquilizers. They often suffer from headaches and the analgesics taken for their relief can be inadequately metabolized, complicating the picture further. The drowsy periods may follow meals with too much nitrogen content, since these patients are particularly sensitive to nitrogenous substances. The rigorous need for a protein-free intake may create psychological problems. This syndrome has been attributed to the introduction of intestinal absorption products directly into the systemic circulation. The blood ammonium is usually raised, but it does not always correlate with the neurological state.

Burn Patients

The psychiatric aspects of extensive burn patients have been largely ignored. Yet a third of the patients with significant burns may develop delirium. Half of the delirium patients were hallucinating and thrashing, half were somnolent. The extensiveness of the burn and its associated metabolic derangements were obviously related to delirium causation. Premorbid psychopathology was also implicated. It would seem that sensory restriction may also play a role with limited mobility and impaired sensory input. Certainly, massive anxiety would be mobilized by the traumatic event and the threat of disfigurement and death.

Intensive Care Units

The ICU may reproduce many of the etiological factors in delirium. The patients are quite sick and vulnerable, and even if delirium is not caused, environmental factors may add to agitation, anxiety, and depression. The cardiac care unit is similar in many ways to the OHRR. There are intravenous (IV) catheters, electrocardiogram (EKG) cables, flashing EKG oscilloscopes with bell alarms (with inevitable false alarms), and an omnipresent defibrillator. A cardiac arrest brings a stampede of house officers. Parker and Hodge have reported delirium in these units which they attribute to sensory monotony. On the other hand, Hackett and Cassem did not find significant

psychopathology. It should be noted that the units vary greatly in environment and personnel. In some converted units there is only curtain separation, while newly constructed units have cubicles and concealed monitoring equipment. The number of patients in a unit also varies. The observation of death and complications in other patients can be particularly distressing with predictable autonomic reactions, which could not come at a worse time. Even patients who deny anxiety related to another patient's death would prefer to be in private rooms.

Caution should be used in applying the term ICU syndrome to delirium in this setting. These patients are severely medically ill, or they would not be there. They are also receiving complex medical regimens. Although we should be aware of environmental factors, our nonpsychiatric colleagues must be urged to explore all possible medical causes for delirium before invoking a purely environmental explanation.

Departure from ICU's can also be traumatic. It is frequently abrupt, and viewed as a rejection with ensuing cardiovascular problems related to increased catecholamine excretion. Symptoms akin to traumatic neurosis can be produced which manifest themselves with delayed insomnia and nightmares. Patients frequently are discharged from the units without adequate recommendations to minimize over- and underactivity.

Treatment

The multifactorial causation of delirium requires a multifactorial therapy. The role of psychic factors does not diminish in the slightest the need for correction of underlying physical abnormalities, which may be brain- and lifesaving. Delirium is a medical emergency; the brain cannot wait. Not only should specific factors related to illnesses and medications be sought, but the general physical condition of the patient, his hemoglobin level, hydration, and nutrition must all be considered. Osier's rule of 1892 still applies, "procure sleep and support the strength." The consulting psychiatrist often finds that the patient with delirium has already been inappropriately treated with a minor tranquilizer or barbiturate. Indeed, the most common recommendation is the withdrawal of barbiturates or minor tranquilizers and substitution by phenothiazines. Barbiturates and minor tranquilizers are only indicated in withdrawal syndromes, and may worsen or precipitate a delirium. On the other hand, chlorpromazine is particularly useful. It should be given 25 mgs. intramuscularly, and repeated as needed. Usually 25 mg. IM (intramuscular), or 50 to 100 mg. by mouth every four to six hours is sufficient. A standing order, to be given when the patient is awake, is generally preferable to awaiting severe symptoms. If excessive somnolence is produced, a less sedating phenothiazine, such as thioridazine or trifluoperazine, can be substituted for part or all of the dosage. The drugs have a potent antipsychotic effect, and provide "chemical restraint" which is far superior to

physical. It may be necessary to assuage the undue fear internists and surgeons have of these medications causing hepatitis and hypotension. Generally the benefits far outweigh the risk. However, a greater risk is that effective symptomatic treatment may dissuade the referring physician from vigorously pursuing the etiology of the delirium once behavioral problems have diminished.

Prevention and therapy should also include minimizing sleep interruption and sensory restriction or overload. An overly sterile, monotonous, instrument-laden hospital room provides a blank screen upon which the patient can project his fantasies. Immobilization is also unnatural and should be avoided. Familiar figures from the patient's life should be available to him as much as is feasible. Stays in OHRRs or ICUs should be as brief as possible. The staff should be helped to provide a warm, trusting relationship.

Psychotherapy visits should be brief and frequent. Recognizing the precarious state of integration of these patients, efforts should be made at support and ego enhancement, rather than at exposing deficits. Efforts should be made to provide cueing, and to reduce the harsh criticisms of performance failures. The psychiatrist must convey that he understands what the patient is experiencing. Patients should be told that they have a reversible condition for which there is appropriate treatment. They can be reassured that there is a

specific, usually correctable stress, and that they are not “going crazy.” They should be encouraged to report unusual experiences to the staff. Encouragement can be provided as recovery begins. After recovery, patients should be given the opportunity to understand and integrate their experience.

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