Dr. Fred Klenner suggests that viral encephalitis can follow head and chest colds. Large doses of ascorbic acid administered by means of the needle can play a vital role in restoring the patient's health. Injected vitamin C, he says, not only destroys the responsible virus but also helps to maintain the integrity of the blood vessels in the brain. He speculates on routes viruses might take to enter the brain.—*R.D.M.*

Virus Encephalitis as a Sequela of the Pneumonias

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Every head cold must be considered as a probable source of brain pathology. Many cases of encephalitis precipitated by an attack of coryza will be of little significance and not recognized clinically. Some, however, will cripple; others will kill. This paper is presented in the hope that physicians will be on the alert for this insidious syndrome first described by Rosenfeld in 1903 under the caption "Brain Purpura or Haemorrhagic Encephalitis."

Many people have needlessly died through indifference on the part of the individual, a parent or guardian, even the physician. The so-called head cold is like a live ember in that it possesses the innate faculty of bursting into a consuming fire with the *next* breath of air pulled through the engorged nasal pathways. Frequently the "down-draft" is like a miniature tornado, transporting the microbes to the trachea as a tracheitis—a burning sensation in the region of the sternal notch. If not challenged with proper therapeutic agents, the main bronchus will be next. From the main bronchial tree the *flames of infection* extend out to the bronchioles as a bronchiolitis and then to the parenchyma of the lungs as a pneumonic reality. Often a pneumonitis exists without demonstrating too great incapacitation of the individual, who continues with his or her usual routine while attempting to alleviate the persisting head cold or nagging cough with a variety of combinations of home remedies. The physician has the responsibility to elicit this information from the patient, since such therapeutic measures will often cloud the true picture. Patients have died following the sudden development of cerebral manifestations, secondary to a slight head and/or chest cold because doctors were not impressed with their findings at the time of the initial examination or even with the history given by the individual, a relative, a friend. This is especially true in children, since children are not professional fakers to the extent that their behavior commands that they be carried for immediate medical consultation. It is better to *rule out* virus encephalitis by diligent observation and the employment of every laboratory procedure available that might lend assistance in the diagnosis rather than to have it *ruled in* at autopsy.

In an attempt to arrive at any definite etiological denominator, one must accept certain established clinical facts which tend to point to a common factor in all cases.

As pointed out by Baker and Noran,[1] in each type pneumonia cerebral complications of a *similar* clinical and pathological nature occur. This immediately speaks against the etiologic organism of the offending pneumonia as the probable agent causing the encephalitis. Baker and Noran suggested the possibility of a toxin responsible for this syndrome since scattered cerebral symptoms may occur in a toxemia secondary to pyrexia in any illness. They concede, however, that since severe cerebral manifestations are precipitated many times after the pneumonic process has subsided, or is only in the developing phase, that some other toxin, one not necessarily associated with the pyrexia but more directly related to the pneumonia and to the individual susceptibility to cerebral involvement. From a review of our own cases it can be stated categorically that in all near fatal illnesses the temperature was essentially normal; that is, one half degree either side of 98.6° F. initially. Ferraro[2] advanced the *allergic* theory, assuming that an allergic phenomenon took place in the central nervous system during the infectious disease. The consistency of the clinicopathologic picture found in these cases, in spite of the wide variety of pathologic organisms involved in the pneumonia, would tend to favor the *virus* concept.

Detection or awareness of this "brain" complication becomes of paramount importance, since severe cerebral residuals often follow relatively mild pulmonary inflammation. Comby, in 1907, was the first to call attention to this interesting *metastatic* sequela of the pneumonias. Although this nonpurulent type of encephalitis may follow every variety of pneumonia, the greater number will be associated with primary viral pneumonitis. This invasion of the lungs as the precursor of the encephalitis is always represented by mixed pathogens. When the pulmonary pathology is predominantly virus in origin, the secondary invaders will usually be found in the main bronchial tree and in the upper respiratory areas. When the pneumonic process is due to the staphylococcus or the pneumococcus the virus as the secondary invader can be present in all parts of the pulmonary system. When influenza is epidemic the pneumonia accompanying will be of the diffuse bronchial type yielding almost a pure culture of pneumococcus. This was the bacteriological and radiological findings during the recent flu epidemic in this area. All are aware of the possibilities of the staphylococcus, especially in infants, when chemotherapy has been pointed at every thing but gram positive organisms, or when "immunity" to *fashionable* drugs has been acquired by the micro-organisms because of the indiscriminate application of such drugs by the practicing physicians.

In a clinical problem such as these cases present, one must speculate on the pathway, as well as the manner, in which the virus gains entrance into the brain. The blood supply to this area definitely plays an important role. The arterial and venous channels as summarized by Wolff[4] from the works of many investigators follow. The cerebral arterial tree, unlike that of many organs, has no hilus from which the vessels plunge into the body of the structure. Blood flowing to the brain through the internal carotid and vertebral arteries are united by the "Circle of Willis" which, with its six large branches, encircles the globoid hemispheres at their base. These trunks then divide into many smaller branches. A few enter the basal ganglia and choroid plexus, but for the most part they spread themselves like a net over the surface of the cortex. Smaller arteries at innumerable points dive deeply into the cortical and subcortical tissues where they anastomose with one another and with others coming through the brain substance from the opposite surface of the hemisphere. The cerebral veins comprise two groups, the internal and external, with incomplete anastomoses between them. The internal group drains through the great vein of Galen, running back directly over the pineal body. The external veins emanate from the region of the insula. Because with growth there is anterior displacement of the frontal lobe, and posterior development of the main mass of the hemispheres, the direction of the terminal portion of the great veins is altered; the anterior veins are thus directed posteriorly and the posterior veins course obliquely anteriorly as they pass to the superior sagittal sinus. The large venous sinuses drain into channels at the base of the skull. The nerve control as given by Starling[5] simply states that the brain, as the master tissue of the body, and acting through the medullary centers, controls the circulation through all other parts of the body. In maintaining normal function the brain requires a certain blood supply which is dependent on the pressure in the carotid arteries and Circle of Willis. If this pressure fails, the function of the brain will be affected and loss of consciousness rapidly ensues. The alarming increased respiratory rate seen in many of the "encephalitic" patients strongly suggests that cerebral compression and/or abnormal *vagal* stimulation is taking place. The depth of the pulmonary pull will also be exaggerated and might be used as an index in determining the type and degree of involvement of the central nervous system. Hyperpnea in such instances is involuntary. It is probable that due to an increase in hydrogen ions in the respiratory center itself,[6] secondary to impaired blood flow through the inflamed lungs, may be the activating factor. This forced and sometimes labored breathing, but not Kussamaul in type, results from insufficient oxygen supply to the respiratory center and in some part to acid production within the center itself. Under abnormal conditions,[7] including various diseased conditions, the possibility of a "frank" acidosis being a potential cause of oedema is quite plausible. This syndrome alone would account for the clinical manifestations of headache, irritability, anorexia, abdominal cramps, weakness. coma and sometimes *death*.

Baker and Noran enumerate five groups, each showing certain definite clinical characteristics which may be of both diagnostic and prognostic significance in relation to this *virus* syndrome: (1) Symptoms of a nonspecific nature (headache, vomiting, irritability); (2) delirious type; (3) convulsive type; (4) lethargic type; (5) hemiplegic type. These groups plus two additional types, namely, (6) blood invasion type and (7) allergic rhinitis type were reported by me in the *Tri-State Medical Journal*, October 1958. This report was made on the basis of actual cases treated in our local hospital without knowledge of the Baker-Noran publication. This factor is emphasized to show the frequency in which this pathology presents itself and to call attention to the "stereo-types" which should make the clinical recognition elementary. Occasionally one will find overlapping of the groups. One case, in an adult, began with convulsive seizures which finally demonstrated paralysis. Irritability and increasing severity of headache over a period of several days was the history given by both our cases showing the delirious type. In spite of this obvious picture, many patients die with the diagnosis *labeled* pneumonia. nephritis, rheumatic fever, cerebral haemorrhage—anything but *virus encephalitis*.

It is possible for the virus to gain entrance into the cerebral structures by several routes: (1) Through the olfactory nerves; (2) direct extension from otitis media; (3) through the portals of the stomach from material swallowed from pulmonary and/or upper respiratory drainage; (4) the blood stream. After arriving in the brain the virus goes through the blood cerebro spinal fluid barrier and/or the blood brain barrier by one of three ways: (1) Electrical charge; (2) chemical lysis of tissue; (3) osmosis. Wittgestine and Krebs, 1926, reported that the *choroid plexus* is impermeable to basic dye while the *capillary system* of the brain, although permeable to acid dye, is much more susceptible for the passage of basic dye. Friedeman and Elkeles in 1930 and Schmid in 1931 demonstrated the existence of a reverse relationship between the blood brain barrier (B.B.B.) and the blood celebro spinal fluid barrier (B.C.S.F.B.) in that by dye experiments it was shown that the B.B.B. is more permeable for basic dye while the B.C.S.F.B. is more permeable for acid dye. Bakay[8] reported that the permeability of the B.B.B. can be changedd by introducing various toxic agents into the blood circulation. The effect of these agents is only temporary and the "barrier" usually regains its normal function within minutes or hours following their application unless the plasma concentration of the toxins is kept at a constant high level. Spatz (1933) found that the penetration into the brain of acid dyes depended on their particle size. Diffusion rather than hydro-dynamic flow constitutes the chief process whereby small molecules can exchange rapidly between plasma and interstitial fluid. Other investigators report that the permeability of the cerebral capillaries rests with its electrical charge. The B.B.B. protects the central nervous system from negatively charged toxins. On the other hand the cerebral capillaries are permeable to substances carrying a positive or no charge at the pH of the blood, while they are impermeable to those carrying negative charge. In recent investigations Chambers and Zweifach[10] emphasized the importance of the intercellular cement of the capillary wall in regulating permeability of the blood vessels of the central nervous system. Many scientists believe that the "barrier" *resides* in the intima of the cerebral vessela and that it possesses selective action in the transfer of certain ions from the blood into the brain.

Case History No. 1: 58-year-old white female seen at her home 24 hours prior to hospital admission. History of slight head and chest cold for period of 10 days. Examination revealed nothing remarkable. Appropriate therapeutic measures taken. Reported much improved 12 hours later. Admitted to local hospital 24 hours following initial visit because of convulsive seizure. Patient experienced three additional convulsions. Admission temp. 100.8° F., pulse 140, Resp. 32. Extremely restless. Was given 24 grams ascorbic acid with 350 c.c. 5D in water I.V. for three times at 8 hours intervals. Digifortis Amp. 1 for 7 times then q 2 h until digitalized. Metrazol 0.1 gm given I.M. q 8 h. Ilosone 250 mg q 4 h as supportive treatment. Four grams ascorbic acid given in orange juice q 4 h. Twenty-four hours following admission patient was awake and rational but completely paralyzed right arm and leg. This cleared completely after 48 hours. Oxygen, nasal, given 5 liters per minute. Lyo-B-C was given with 6 grams ascorbic acid I.V. daily for 8 days. The patient was well of her virus infection by the fourth hospital day. She was however a severe cardiac and because of a diet psychosis for years required weeks of hospital stay to return her to her usual routine. Classical pellagra was also treated and corrected during this hospital admission.

Case History No. 2: 23-year-old white male. Seen in emergency room local hospital in semicoma. Friends stated that he was found unconscious in telephone booth. Temp. 98.6° F., pulse 130, respirations 34 per minute, extremely labored. Pupils dilated. Subsequently patient narrated that he had had a cold for two weeks. Experienced headache for period of five days prior to hospital admission. He had consulted another physician the day of admission because he could no longer endure the severe headache which failed to respond to excessive doses of usual remedies. He was given 30 grams of ascorbic acid in 350 5D water I.V. Approximately 30 minutes following admission and shortly after fluids were started he became violently disorientated requiring four men to hold him on the bed. This continued for about five hours after which his recovery was uneventful. The initial order for ascorbic acid was repeated at 8 hour intervals for five times. Following the intravenous medication, ascorbic acid was given 4 to 6 grams in juice every 4 to 6 hours. His WBC was 7000 with a normal differential. He was sent to a teaching hospital by request of his parents after 6 hospital days where the impression of viral encephalitis was confirmed. He received no treatment at this second institution and was discharged to his home following completion of his examination. Achromycin V 250 mg. was given every 4 hours for 12 times.

Case History No. 3: 22-year-old male first seen in emergency room of local hospital where he was reported to be in an unconscious state. Upon arrival at the hospital, however, I found the patient on the floor, being held down by seven men while an attempt was made to bind his less and arms with sheets. This did not hold patient and within minutes he was loose, up on his feet and swinging wildly at anything that came in his way. He was subdued by grasping one arm at the wrist and the other hand of the subduer was “attached” to the patient’s hair which was pulled with force in a backward direction. With this hold the patient allowed himself to be placed on a stretcher and arms and legs tied to each corner with sheets. After recovery the patient did not remember this episode. He remained rather agitated for about four hours after which time he was a model. We elicited the history on the second day that he had been irritable for the entire week before this incident; he could not get along with anyone. On the day of hospital admission he saw a second physician because he believed his severe abdominal pain might be associated with a recent haemorrhoid operation. He had had a dull to severe headache for several days but attributed this to a sinus condition, although he remembered telling a relative that the pain was different than what he usually experienced. He did not have the prescriptions filled that were given to him by the surgeon. Later the same day he accompanied a friend on a short trip during which time he suddenly developed extreme head pains, severe nausea and profound weakness. He telephoned a relative to come get him and take him home. He collapsed as he left the telephone booth and was believed dead. The ambulance driver confided that he too believed the boy dead and brought him to the hospital for confirmation. Temp. was 98.4° F., pulse 146, respirations 28 per minute. He was given 50 mg. thorazine by needle in an effort to control his restlessness. Ascorbic acid was given in massive doses, 100 grams intravenously the first 24 hours. Subsequent doses consisted of 4 grams in juice q 4 to 6 hours. Penicillin was employed for secondary invaders. He experienced severe nose bleed on the 6th hospital day requiring a classical pack. Calcium gluconate 10 c.c. was given I.V. for two times with the thinking that high doses of ascorbic might have removed calcium ions in excess by way of oxalic acid as the calcium salt.

SUMMARY

Virus encephalitis as a sequela of the pneumonias is more common than the literature would suggest. This error exists because physicians no longer take or have the time to read and reflect. This error exists because physicians are inclined to make their diagnosis from laboratory reports rather than with the use of the stethoscope and their brain. There are many pathological conditions in which similarity tends to mislead. If this paper provokes those physicians who read it to consider the possibility of cerebral complications with lingering head and/or chest colds, our efforts will have been rewarded. We must not gamble with the simple head cold.

I cannot but wonder if in the picture portrayed here there lies the factor of "genetical error." Certainly in both cases described as presenting delirious manifestations there is sufficient evidence to warrant such a hypothesis. All the factors presented as an explanation could still follow, their realization being precipitated due to fault in genetics.

The cases that we have seen and successfully treated definitely follow a set pattern so stereotype that once looked for will never be forgotten. Two of our cases demonstrated hemiplegia; five cases had convulsive seizures; four cases abruptly started with stupor or were of the lethargic type; three cases started with a severe shaking chill. Strangling during the course of normal eating and definitely due to nerve paralysis, one case. Many other cases represented the non-specific type and I am sure many, many more cases of a minor nature went undetected.

There is much information available which indicates that the oxidation rate and vascularity may be related. Oxygen consumption of the brain is large, ranking the cerebrum among the more actively metabolizing organs of the body. Interference with the blood supply of the central nervous system can be quickly disastrous, since the brain cannot accumulate an oxygen debt.

The possible routes of invasion by the virus have been outlined along with the manner in which the virus gains entrance into the brain substance.

The importance of the intercellular cement of the capillary wall in regulating permeability of the blood vessels of the central nervous system would suggest also the *importance* of administering large doses of ascorbic acid in order to maintain the integrity of these structures. Especially must this be true if the "barrier" to the brain is associated with the intima of the blood vessels. Large doses of ascorbic acid are necessary also as a chemical to destroy the virus organism. Recently I treated a seven-year-old child, off and on over a period of six weeks, for influenza like symptoms. Therapy included one of the mold derived drugs, sulfadiazine, and moderate doses of ascorbic acid. On three different episodes this type of therapy was dramatically effective. When the child became ill for the fourth time, the administration of the above antibiotics had no reversing action. On the third day the child suddenly became lethargic, began to run as much as 102.6° F. At this point all medication was discontinued except that I began to give six grams ascorbic acid intravenously every 6 hours. During the same time 10 grams ascorbic acid were given by mouth. The recovery was spontaneous in 24 hours. I had ample opportunity to observe this case—the child was my son.

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