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CREUTZFELDT-JAKOB DISEASE

A CASE REPORT, WITH SPECIAL ATTENTION TO THE ELECTROENCEPHALOGRAM IN THIS DISORDER AND TO ITS POSSIBLE RELATIONSHIPS TO KURU, SCRAPIE AND «MAD COW DISEASE»

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SUMMARY — A case of Creutzfeldt-Jakob disease in a 58-year-old Brazillian cattle rancher and businessman is presented. The EEG was normal, which is consistent with the fact that it was made during the first half of his illness; in a later stage suppression of normal rhythms by slow moderate voltage waves would be expected. The resemblances of kuru, scrapie and "mad cow disease» to C-J disease are discussed. In each of these 4 illnesses the patient or affected animal (scrapie and «mad cow disease") (a) has a widespread spongiform encephalopathy and consequent dementia, myoclonic epilepsy and cerebellar and corticospinal symptoms. (b) Each illness is caused by a virus (or virus-like organism called a PrP or prion) which is unusually resistant to heat and entirely resistant to ultraviolet light and x-rays. (c) This causative agent can be transmitted to other mammals by intracerebral injection or, in the proved cases of 3 of them, by the oral route. Unresolved questions about C-J disease include the following: Are C-J disease, kuru, scrapie and "mad cow disease" essentially similar illnesses caused by the same virus or by subtle variants of it? What is the incubation period of C-J disease, and does its virus exist for long periods of time in some asymptomatic persons, some of whom may never become neurologically ill? How does this virus enter the bodies of most persons with C-J disease, and why does the clinical disease characteristically occur only in middle age?

KEY WORDS: Creutzfeldt-Jakob disease, spongiform encephalopathies, electroencephalography.

Doença de Creutzfeldt-Jakob: relato de um caso, com atenção especial ao EEG nesta doença e às suas possíveis relações com kuru, scrapie e "a doença de vacas malucas»

RESUMO — Um caso de doença de Creutzfeldt-Jakob num fazendeiro e empresário brasileiro com 58 anos de idade é registrado. O EEG foi normal, o que está de acordo com o fato de que o exame foi feito durante a primeira metade da sua doença; num período mais avançado, a supressão dos ritmos normais por ondas lentas de voltagem moderada seria esperada. As semelhanças da doença de C-J, kuru, scrapie e "a doença de vacas malucas" são indicadas. Em cada uma destas 4 doenças o doente ou o animal (scrapie e "a doença de vacas malucas") (a) tem uma encefalopatia spongiforme difusa e, consequentemente, demência, epilepsia mioclônica e sintomas cerebelares e corticospinais. (b) Cada doença é causada por um vírus (ou um organismo semelhante a um vírus, chamado um PrP ou prion) que é muito resistente ao calor e completamente resistente à luz ultravioleta e aos raios-X. (c) Este vírus pode ser

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transmitido a outros mamíferos por injeções intracerebrais e, em casos verificados em 3 destas doenças, oralmente. Problemas que ainda têm que ser resolvidos são os seguintes: São a doença de C-J, kuru, scrapie e "a doença de vacas malucas" moléstias basicamente semelhantes produzidas pelo mesmo vírus ou por variações sutis dele? Qual o período de incubação da doença de C-J e pode este vírus viver durante períodos prolongados em pessoas assintomáticas, entre estas algumas nunca ficando neurologicamente doentes? De que maneira entra este vírus no corpo da maioria das pessoas com a doença de C-J e porque esta doença em geral acomete somente pessoas de meia idade?

PALAVRAS-CHAVE: doença de Creutzfeldt-Jakob, encefalopatias espongiformes, eletrencefalografia.

The disorder now called Creutzfeldt-Jakob disease was delineated between 1920 and the early 1950s by the German psychiatrists Alfons Maria Jakob (1884-1931) and Hans Gerhard Creutzfeldt (1885-1964). During the 1950s articles began to be published on this new clinical entity [1,12] and toward the end of the decade its EEG findings were first reported [1,16]; from the 1960s onward the EEG in this condition has from time to time received further attention [11,13,14,20]. Reports of C-J disease in the Brazilian literature began in 1971 [19] and have at intervals continued to appear since then [3,4,7,10,15,17,19,20].

At the present time the symptomatology, course and histopathology of the disorder are well understood, but other features of it have as yet not been clarified. These include the way in which the causative virus enters the patient's body, its incubation period, the nature of this virus and possible relationships of C-J disease to a similar disease in humans (kuru) and 2 like diseases in animals (scrapie and «mad cow disease»).

CASE REPORT

The patient AFM is a 58-year-old cattle rancher and businessman whose first symptoms appeared in June, 1991. He is married with 3 adult children and has lived all his life in south Bahia on cattle ranches and in 2 towns in this region. No one in his family has ever had a disorder similar to the one reported here. The first symptoms consisted of difficulties in speaking, reading and writing; observers were less certain about whether he had trouble understanding things that were said to him at this time. These problems began suddenly and increased over a period of 2 weeks. However he continued to carry out many of his usual activities despite them. In September, 1991 he was evaluated in a neurological service in São Paulo. A routine neurological examination revealed only his aphasias. Cerebrospinal fluid examination, computorized tomography and magnetic resonance image were normal. An EEG was read as showing "left temporal dysrhythmia", but the nature of this dysrhythmia was not specified; neither slow waves nor spikes were seen. A rCBF study revealed frontal hypoactivity and left (the patient is right-handed) occipito-parietal hypoactivity. No diagnosis was reached, but the patient's family was informed that the most probable pathological process was diminished blood flow to the affected areas of the brain due to narrowing of cerebral arteries and perhaps tiny terminal obstructions in them. The patient was placed on a low salt diet and weight loss was advised; moderate exercise with long walks was recommended. He was placed on aspirin, 250 mg 4 times a day and alprazolam, 0.25 mg twice a day. It should be noted at this point that the patient had for many years been overweight; in early 1990 he had weighed 150 kg but by medically supervised dieting had dropped to 125 kg by June, 1991 when his present illness began. This weight loss occurred after his family physician found him hypertensive and put him on a regimen of metoprolol, 100 mg each day in addition to his diet. He had been a heavy smoker but had stopped in 1985.

During the following 3 months the patient became steadily worse. His communication difficulties increased and in a fluctuating manner he became more confused and disoriented. He was continually restless, and at times agitated; he was worse at night, often wandering about his house all night and sleeping fitfully at intervals during the day. By December he was vocationally and socially incapacitated. In early January, 1992 his family took him for

neurological evaluation to Recife where he was found to have a blood pressure of 140/85, no carotid bruits, a normal chest x-ray, a normal electrocardiogram, a normal complete blood count, a uric acid level of 5.3, a blood sugar of 84 and a cholesterol level of 176. Transesophageal echo examination showed a normal left atrium and a small enlargement of the left ventricle. The consultant in Recife recommended evaluation at the Presbyterian Hospital and Columbia University Medical Center in New York to obtain a definitive diagnosis. The patient's family accepted this recommendation and a physician from Recife agreed to accompany them to New York to serve as medical interpreter to both the American physicians and to the family.

In New York the patient was found to have moderate semantic paraphasia; even with the aid of the medical interpreter the examiner was uncertain of its extent. A routine neurological examination was unremarkable; the normal findings included pursuit muscle movements, fine muscular coordination, muscle bulk, muscle tone and strength, rapid alternating movements, deep tendon reflexes, flexion and extension movements of all limbs, finger to nose movements, heel to shin placements and thumb tapping with the index finger. The patient at this time was still able to cooperate in such tests. The consultant felt that the evidence pointed to a vascular problem with decreased blood flow to the affected brain areas, and to explore this possibility further ordered an angiogram. The radiologist reported that the angiogram seemed to indicate arteritis of the middle cerebral artery and its branches on the left side. However, still unsatisfied, a brain biopsy was performed to clarify the picture. In his final report the consultant stated that the results of the brain biopsy came as a surprise, revealing a disease he had not thought of. Beause of the absence of tremors, myoclonic epilepsy, and signs of cerebellar and corticospinal involvement, the American examiner, as well as the previous Brazilian neurologists, had not considered the possibility that the patient had C-J disease.

At biopsy 2 pieces of cortical tissue, taken sufficiently forward in the left temporal lobe to avoid accentuation of the patient's aphasias, were removed. They measured 1.4 x 0.6 x 0.7 centimeters by 1.0 x 0.5 x 0.4 centimeters. They were unremarkable on gross examination. Microscopic examination revealed marked spongiform degeneration throughout the cortex, it being most severe in the lower layers. Small and large vacuoles were present throughout the neuropil and many were perineuronal in location. There was much astrocytosis and proliferation of microglial cells in all cortical areas. The vascular structures, adjacent white matter and leptomeninges were normal and no amyloid plaques were found. The 2 pathologists who examined the slides felt they clearly indicated C-J disease.

Further tests were not done, but the New York consultant recommended another EEG after the patient returned to Brazil, as an evaluation of the extent of the patient's ongoing deterioration. He had doubt that an EEG could be satisfactorily done on such an agitated patient by EEG technicians who did not speak his language.

On March 11, 1992 the patient's family brought him to us for the recommended EEG. A formal neurological examination on him would have been impossible at this time because of his increased restlessness, which amount to agitation at times. However it could be noted that he had no tremors or abnormal movements. His aphasia was unusual in that each brief set of words or fragment of a sentence in isolation made sense, but these fragments were strung together in such a way that to a casual observer he was incomprehensible. It seemed probable that the things said to him were similarly unintelligible. However the members of his family and a few others who were in daily prolonged contact with him could sometimes grasp, from his words and gestures, what the wanted to convey. The patient had all his adult life been accustomed to direct the activities of others and carried this personality trait into his organic brain state, becoming impatient if his needs or wishes were unheeded and setting about to do himself the thing he wanted done.

The things that happened in our attempts to do an EEG on the patient throw some light on the nature of his receptive and communicative aphasias and hence these details will be given. The first attempt, which lasted about 20 minutes, was unsuccessful. He could not be persuaded to lie down, to permit placement of the electrodes and to shut his eyes. After abandonment of this attempt the patient, accompanied by a long-time friend and a chauffeur he had had for many years, was taken by his family to a ranch he had about 45 kilometers from the hospital. A short time after arriving there, when he was alone with his friend and his chauffeur, he succeeded in communicating to them that he wanted to return to the hospital and have the test. This time both our EEG technicians worked together in placing, and during the examination several times replacing, the electrodes and running the

machine. They and the friend and chauffeur, who were allowed into the laboratory, talked and a few attempts to rise from the table, an 11-minute EEG was obtained and about 70 persuasively throughout the examination. Despite frequent movements of his head and arms per cent of it was satisfactory for interpretation. A sample of it is shown in Figure 1.

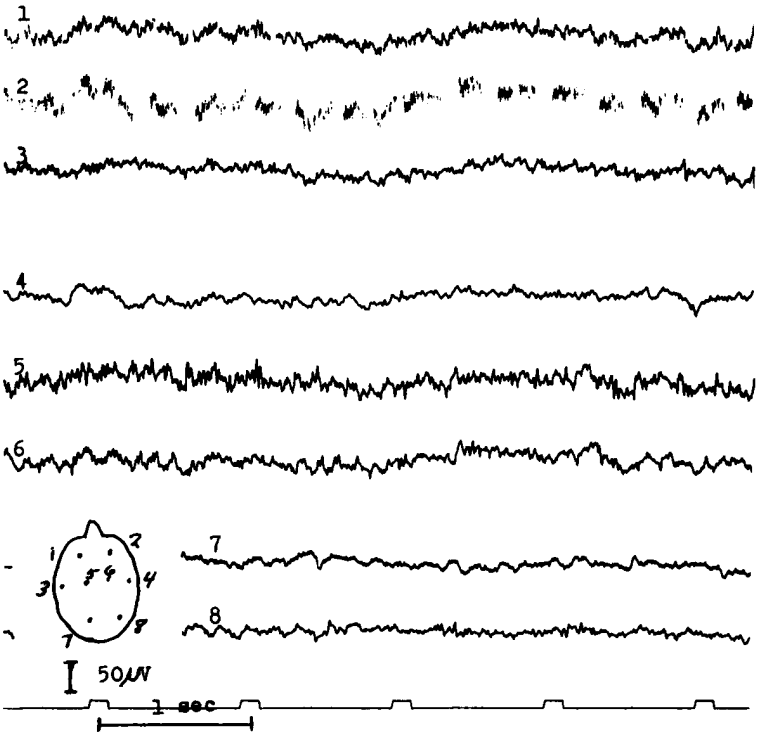

Fig. 1. A low voltage external current is superimposed on the right frontal tracing and there is here also intermittent contact with the paper. These defects were uncorrectable due to the necessity of proceeding in an uninterrupted manner with a difficult patient (see text).

The EEG, made in our usual manner, follows the monopolar conventional, or Illinois, method with ear electrodes as the reference sites; as a small approximation to the 10-20 International, or Montreal, method, the examination is stopped at midpoint and the temporal electrodes are bilaterally moved forward to the anterior temporal positions, giving a total of 10 sampled areas.

This EEG is characterized by low voltage fast activity in all areas during the entire examination. Beta rhythms, at 20 to 24 cycles per second, predominate. Alpha activity, at 9 to 12 cycles per second, are occasionally seen in the temporal and parietal areas during the test. No theta activity, at 4 to 7 cycles per second or delta activity, at 1 to 3 cycles per second, occurs at any time throughout the examination. This is a normal EEG; low voltage fast patterns are common in healthy persons in late middle age *8,9,13.*

COMMENTS

THE EEG IN C-J DISEASE

Kooi[14] writes that in the early stages the EEG in C-J disease is normal. As the disease progresses there are occasional bursts of 4 to 7 cycle per second theta activity and in late stages there often are bilaterally simetrical 1 to 2 cycle

per second delta waves of high voltages. Such waves may be more pronounced on one side than the other. Alone among electroencephalographers, he describes notches at the apexes of these delta waves, giving a diphasic or triphasic appearance. In the terminal phase of the disease voltage of the slow waves decreases. However he notes that some C-J patients have normal EEGs throughout their illnesses. Bannister [2] agrees with Kooi on all points except the diphasic or triphasic nature of the delta waves.

Kiloh and his coworkers [13], citing Nevin [18], report that there is a gradual replacement of normal rhythms by diffuse low or moderate voltage slow activity. Gordon and Sim [11] report 4 cases; one had a normal EEG, 2 had 2 to 5 cycle per second waves of moderate voltage, and 1 had spiking (they are the only writers who report spikes). Lesse, Hoefer and Austin [16] agree in general with the above writers on the EEG in C-J disease, and Brazilian neurologists [7,10,15,17,20] have found similar EEGs in their patients.

THE CAUSATIVE AGENT OF C-J DISEASE

It is now clear that C-J disease is caused by an atypical virus [2] which has been transmitted to higher primates and rodents by intracerebral injection of brain tissue extracts from C-J patients. The infected primates and rodents in time develop spongiform encephalopathy and eventually fatal symptomatology that are similar to the disease in humans. This agent is a single molecular protein, sometimes designated as PrP; the term prion is at time used for it. The way, or ways, in which persons usually become infected with this virus and in time develop C-J disease are not known, but it can be recovered from the cerebrospinal fluid and brain tissues of these patients.

C-J disease occurred in 4 young adults who as children received injections of growth hormones produced by human pituitary glands (removed shortly after the deaths of the donors), and as a result human growth hormone preparations of this nature are now banned in the United States; biosynthetic growth hormones are used in their place. This virus has also entered humans through organ transplant operations, in time causing C-J disease. In still other cases reported in the literature this agent was transmitted accidentally to people by contaminated cerebral electrodes during neurosurgical procedures. This last fact led to statistical studies of C-J patients, and they were found to have in their life histories a much higher incidence of neurosurgical interventions than persons in the general population.

The PrP, or prion, is very resistant to heat, formalin, ultraviolet radiation and x-rays. It can be killed only by autoclaving with steam for 1 hour or by immersing it in sodium hydroxide for an equal period. Laboratory workers who deal with brain tissues, cerebrospinal fluids and other organ tissues of C-J patients have been advised to be circumspect in their handling of such materials.

THE CLINICAL CHARACTERISTICS OF C-J DISEASE

Age of Onset and Duration. The peak age of onset of this disease of worldwide distribution is the late 50s, and it occurs equally in men and women, but authorities differ a good deal in their statements about the length of time between the onset of symptoms and death. Some state that death occurs in 3 to 6 months in most cases, but others put 12 months as the usual upper limit. Others who have reviewed large numbers of C-J patients in the world literature state that though death usually occurs within a year it may exceed 2 years in from 5 to 10 per cent of cases. As in patients with other kinds of dementias such as Alzheimer's disease, the cause of death often is hypostatic pneumonia, infected decubitus ulcers or cardiovascular illnesses which occur before the brain process runs its full course. Our patient, who has not developed any symptoms beyond those of cerebral cortical involvement during 15 months (the time of this writing), is clearly going to be a long surviver for C-J disease.

Diagnostic Procedures. Brain biopsy is the only procedure which allows C-J disease to be diagnosed with certainty; without it the clinician can only

speculate. The characteristic spongiform encephalopathy with neuronal loss, vacuoles, astrocytosis and, in some cases, amyloid plaques, is found in no other human disorder.

All other tests which may be abnormal in C-J disease are nonspecific. Computerized tomography, the various magnetic resonance techniques and the EEG become abnormal only in the advanced stages of the illness when severe brain pathology has caused atrophy and distortions of tissues. The cerebrospinal fluid is normal. The causative agent, the PrP or prion, can be found in the cerebrospinal fluid and in biopsied brain tissue, but its demonstration requires such sophisticated, special methodology and equipment that this is not practical in day to day clinical work.

Symptomatology and Clinical Course. This illness always begins with mental confusion produced by the initial involvement of the cerebral cortex. Deterioration of hygiene and grooming, memory defects, disorientation, nighttime restlessness and defects of judgement and general information occur in almost all cases. As in other cerebrocortical dementias, such as Alzheimer's disease and cerebral atherosclerosis, the patient's lifelong personality tends to color the specific mental and interpersonal problems he has. As he struggles to adjust to his environment with continually fewer cortical cells at his command, the person who was introverted before he became sick tends to become withdrawn, mute and seclusive, and the extrovert tends to become boisterous and hyperactive in a disorganized manner. Our patient, as we have noted, was all his life an ebullient businessman who usually directed the activities of others in both his personal and vocational life and he carried these qualities in a caricatured way into his dementia.

The most common symptoms of noncortical involvement are tremors and myoclonic epilepsy; these 2 findings often alert the neurologist to the fact that his patient is not suffering from some common type of chronic brain syndrome such as Alzheimer's disease. Such symptoms usually begin during the first 3 or 4 months of the clinical illness. Next in frequency come abnormal movements and incoordination caused by cerebellar damage as the disease spreads to other brain areas, and corticospinal involvement often is indicated by abnormal plantar reflexes, clonus and increased deep tendon reflexes. Basal ganglia symptomatology is common with cogwheel rigidity, resting tremors and postural abnormalities. In a small number of cases the anterior horn cells and the nuclei of the cranial nerves are affected; optic nerve impairment may cause visual field defects and blurring of vision.

There is no specific treatment. Medication to reduce agitation, particularly at night, may be useful, and the various nursing techniques employed in patients with dementia are helpful to both the patient and his family in his total management.

C-J DISEASE, KURU, SCRAPIE AND «MAD COW DISEASE»

Three other spongiform encephalopathies are well known. One of them, Kuru, occurs in humans, and 2 others, scrapie and «mad cow disease», occur in animals. Because of their striking resemblances to C-J disease in symptomatology, brain pathology and other aspects, we shall consider them briefly. They raise interesting questions about all 4 diseases.

Kuru. Kuru[2] is a slowly progressive, fatal central nervous system disease that causes dementia, personality changes, emotional instability with inappropriate emotional responses, ataxia of the limbs and trunk, dysarthria, clonus, tremors, muscular rigidity and strabismus. In it spongiform encephalopathy with loss of neurones, vacuoles, astrocytosis and, in some cases, amyloid plaques attacks the cortex, cerebellum, basal ganglia and corticospinal tracts. Death is often by hypostatic pneumonia and infected decubitus ulcers after a course of 3 to 12 months.

Kuru is caused by a virus that is similar to that which causes C-J disease and scrapie (to be discussed below). It occurs only in the Fore and neighboring tribes in the highlands of New Guinea in Australasia who contract this illness

by eating the brains of deceased relatives in religious rituals. This virus has been transmitted by intracerebral injections of extracts from the brains of persons suffering from kuru to higher primates and rodents in whom it causes a like illness with spongiform encephalopathy. The incubation period of chimpanzees so infected is always longer than 1 year. Kuru is now rare because of the efforts of government officials in New Guinea to stamp out cannibalism.

Scrapie. Scrapie [22] is a progressive, fatal central nervous system disease of sheep that has been known to sheep breeders in Scotland and northern England for more that 200 years and has occasionally spread to France and Germany where it is called tremblante du mouton and rida. In this century outbreaks of it have occurred in the United States, Canada, Australia, South Africa and India, but it has never become widespread in those countries. An affected sheep becomes excited and behaves in other altered ways. Tremors of the head, weakness and incoordination of the limbs, more marked in the hind quarters, and a general wasting occur with death ensuing in 2 to 6 months. A sheep with scrapie often rubs its limbs against trees, fence posts and other sheep and may gnaw at its legs. Between 5 and 60 per cent of the sheep in a flock, depending on the breed, may acquire it; goats are 100 per cent susceptible but less frequently are affected by this disease.

Scrapie is usually acquired by direct transmission from parents to offspring very early in life, but the infection may also be transmitted orally or by contact with sick animals. It rarely appears in a sheep that is less than 2 years old and thus an infected flock may remain to some extent economically viable. The causative agent is a virus or virus-like organism which has not yet been identified and studied by electron microscopy. It survives exposure to ultraviolet light, is unusually resistant to heat and does not produce antigens. It has been transmitted by intracerebral injection to hamsters, rats, mice and minks, in whom it produces a similar illness and spongiform encephalopathy, and from these animals it has been transmitted back to sheep, again causing scrapie. In experimental tests oral transmission has also been demonstrated.

The brain pathology in scrapie consists of spongiform changes with neurone loss, vacuoles and astrocyte proliferation in the cortices of the cerebrum and cerebellum and in lower brain centers. Brain biopsy is the only certain diagnostic procedure and there is no useful treatment.

«Mad Cow Disease». A hitherto unknown disease began to appear in cattle in England in 1991 [21]. Affected animals, who developed tremors, altered behavior and staggering gaits, died after several weeks or a few months, and autopsies revealed spongiform encephalopathy. The similarity of this brain pathology to that of sheep with scrapie, along with likenesses in symptomatology, led to investigations which revealed that these cattle had eaten dietary supplements which contained the brains of sheep . This illness attracted much attention in English tabloid newspapers and on British television, where it was dubbed «mad cow disease», and this publicity caused a noticeable decline of beef consumption in Britain and a Freench ban on the importantion of British beef. The British minister of agriculture toured the United Kingdom eating beef and reassuring people that it was safe for consumption. By early 1992 the situation was back to normal in all respects, the inclusion of sheep brain tissue in catttle feeds having been terminated. The veterinary name for this illness is bovine spongiform encephalopathy, but the popular term «mad cow disease» has become fixed for it and is usually employed even in veterinary and scientific discussions, just as the rarely utilized term ovine spongiform encephalopathy is the technical name of scrapie.

During 1992, however, cases of spongiform encephalopathy began to occur in cats in Britain, and in 1 puma in a zoo, and the symptomatology of these felines is similar to that of other animals with spongiform encephalopathy; at the time of this writing 1 cat per month is dying of spongiform encephalopathy in Britain. It is suspected, but not proved, that these animals ate cat food commercial preparations containing sheep or cattle brains; since such cat food may in canned or frozen form remain for long periods in households before being used a continuation of this illness for some time is expected.

UNANSWERED QUESTIONS ABOUT C-J DISEASE

Are C-J disease, kuru, scrapie and «mad cow disease» caused by the same or quite similar viruses?

The virus, or virus-like, agents which cause these 4 diseases, in addition to producing spongiform encephalopathy and illnesses which resemble each other, have other similarities. They are unusually resistant to heat, are completely resistent to ultraviolet light and x-rays and do not produce antigens. All of them can be transmitted to other animals, either rodents and higher primates or animals similar to themselves. Kuru, scrapie and «mad cow disease» can be transmitted orally and C-J disease can be transmitted by intracerebral injection. It would be interesting to know if C-J disease can be transmited **orally** to higher primates, sheep and cattle.

What is the incubation period of C-J disease?

The length of time between the entry of the causative agent of C-J disease into a person and his development of the clinical disease is unknown. However, fragments of data suggest that it may be years or decades. The 4 young adults who had injections of contaminated human growth hormone in childhood did not develop C-J disease until 1 or 2 decades later and persons who acquire the virus through contaminated electrodes or neurosurgical instruments seem to have an equally long latency period. Sheep in most cases get the virus of scrapie from their parents at birth or in the early weeks of life but do not become ill with the disease until 2 years of age as a rule. When the virus of kuru is introduced into a higher primate a similarly long latency period ensues before the animal becomes neurologically ill.

There is the allied question about why C-J disease characteristically is an illness of middle age. Since the causative agent can produce C-J disease at any time from early adulthood onward when it is introduced by human growth hormone injections, organ transplants and neurosurgical contamination it would seem probable that the usual time of onset of this disease would not be concentrated in one life period, middle age, but would at least to some extent be more evenly spread over the life spans of these patients. The alternatives are to speculate that the virus in some obscure way usually enters the patient's body during his 40s or early 50s or that some particular physiological change during late middle age makes the body susceptible to a disease caused by a virus which has been in it for decades.

These considerations lead to another problem. The fact that the virus may be acquired by hormone injections, organ transplants and neurosurgical interventions suggests that it is much more widely disseminated in asymptomatic persons in the general population than the extreme rarity of C-J disease would indicate. Injections of human brain extracts, organ transplantations and neurosurgical procedures are statistically rare occurrences in the human population at large and the chance that C-J viruses would be contracted through them is minuscule unless such viruses are much more prevalent in people than we have until now felt they are. This in turn suggests that some carriers may never develop C-J disease even if they live into old age.

One way out of this dilemma is to speculate that the majority of persons with C-J disease are never so diagnosed, but die with diagnoses of atypical Alzheimer's disease or cerebral atherosclerosis or some other neurological illness. This could be the case in those areas of the world in which most patients do not have access to skillful neurological care. Indeed if our patient had been one of his own cowboys or factory workers it is improbable that he would have been correctly diagnosed. Such an argument however does not solve this problem as it applies to most Northern Hemisphere countries where a patient with rapidly evolving dementia, myoclonic epilepsy, cerebellar signs and corticospinal symptoms is as a rule seen by an experienced neurologist at some point in his illness.

How does the causative agent enter the body of a C-J patient?

The way in which most C-J patients are infected is not known. Since in kuru and «mad cow disease» the virus is orally ingested (and oral infection also occurs in some sheep with scrapie), the question rises as to whether C-J pa-

tients are similarly infected. Review of the medical literature gives no help in this regard since dietary histories are never included in case reports or in general reviews on this illness. A relevant dietary history moreover woud have to cover eating habits over many years or even decades, before the onset of the illness. Vocational histories of equal duration, which also are not given in case reports, might be revealing. It woul be interesting to know if C-J patients often had much contact with sheep, goats and cattle in their work, as our patient did. Since both the authors of this article have known the patient and members of his family since the 1960s his vocational history was known to us; he had for about 4 decades worked much with cattle and had occasional contacts with sheep and goats. Members of his family were unable to say with certainty whether he had ever eaten the brains of cattle and sheep but felt that it was probable that at least a few times in his life he had done so. Such dishes are considered occasional delicacies in this culture, especially when skillfully sauted in palm oil.

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