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THE NATURE OF CONCUSSION*

BY

GEOFFREY JEFFERSON, M.S., F.R.C.S.

Professor of Neurosurgery, University of Manchester; Hon. Neurological Surgeon, Manchester Royal Infirmary and Salford Royal Hospital

The approach to the interpretation of concussion through its history presents a kaleidoscopic panorama in which succeeding generations are seen attempting to solve the same problem in the light of the scientific knowledge available to them; the same patterns of thing recur in a new setting. The first solutions were vibratory and oscillatory, and were suggested by contemporary new work in physics; they were what we should now call neurogenic, although the neurological knowledge on which any satisfactory conclusion could be reached was still to come. We shall do well to remember that each succeeding explanation offered was in accord with the best information in physics then available. However incorrect it may seem to us, it was satisfactory to a large number of contemporaries, and bore the imprimatur of the leaders of thought of the day. Some 80 years ago the oscillatory theories were abandoned in favour of a new vascular hypothesis. It was suggested by the work of Goltz, who had impressively demonstrated that the effects of shock were caused by a paralytic vasodilatation.

In 1870 Hermann Fischer, in a paper that was to become famous, discussed a case of head injury shown at a clinical meeting the day before. He asked, "What is the anatomical basis of the picture?" Various people had made suggestions, usually on gross anatomical evidence. Thus Rokitsky (1856) had been satisfied that capillary apoplexy at the site of the injury, and maybe elsewhere, explained all the signs; and Nélaton (1847) had held a similar belief. Actually punctate haemorrhages were first described by Richard Bright (1831), who stated specifically that he did not think that they would account for the symptoms of concussion or coma. Fischer's own explanation was of a physiological kind, because in two cases that he had observed he found nothing but cerebral anaemia with congestion of the surface vessels and the dural sinuses. "You will ask," he said, "what sort of queer disease picture is this that to-day threatens the patient with the severest symptoms, all of which to-morrow will have passed completely away." He suggested, but immediately rejected, reflex vessel spasm as a possible cause of this anaemia, and replaced it with the postulate of long-continued vasoparalysis. Seven years later Ludwig Witkowski, after having first accepted Fischer's theory of vasoparalysis (and it is a remarkable error of medical bibliography that Fischer is usually credited with having postulated vasospasm), finally rejected it in favour of a neurogenic causation, its localization unspecified. Bergmann went through the same phases, while Kocher (1901) in his unnecessarily long and verbose book can be held to support all theories. Vasospasm at no time had reputable supporters,

because the physiologists had proved that there were no vaso-constrictor nerves on the cerebral vascular tree—a belief supported by Leonard Hill, and not shattered until the work of Forbes and Wolff (1928) and of M. Riser (1936) and Villaret *et al.* (1936) provided the needed correction. Ricker (1919), again, postulated a vasoparetic explanation with prestasis and focal softening. In the meantime the theory of mechanical arrest of the circulation by an instantaneous rise of intracranial pressure at the moment of injury, suggested first by Strohmeyer (1864) and brilliantly put forward anew by Trotter in England (1932), won an army of adherents. Trotter stated that cerebral anaemia was the cause of concussion, which he defined as a state of paralysis instantly induced but with a strong natural tendency to rapid and spontaneous recovery and not necessarily associated with gross damage. Longer periods of unconsciousness were attributed to contusion, but as to contusion of what (except of the brain generally, with possible local bruising and burstings) Trotter was silent. This will be recognized as a return to the neurogenic theory, although Trotter always spoke disrespectfully of those who believed in molecular commotion with widespread synaptic breaks—as well he might if the phrase is interpreted literally. In England, C. P. Symonds (1940) and I were critical of the vascular theory.

The apparent paradox arises, from a consideration of the most important contributions of the last two centuries, that in the main, however much the interpretations disagreed, the observations were correct. Although a great deal was added to the data of cerebral injury the anomaly remains that the most striking feature, the unconsciousness, was left unsolved. We shall see that the reason lay in the inability of the investigators to grasp the fact that commotion of the brain may upset its actions for much longer than a moment, the disturbance enduring longer and longer according to the severity of the concussive force. (I shall have more to say of this matter in a moment.) Nor could the majority conceive that anything below a cortical level could interfere with consciousness.

Experimental Effects of Concussion on the Brain-stem

The effects of injury showing themselves so often by alteration in the pupils, in the frequency and depth of respiration, in the pulse rate, blood pressure, and low-level somatic reflexes (the corneals, the pharyngeal, laryngeal, and swallowing), focused the attention of some workers on the brain-stem and on possible means by which such a low-level injury could come about. Hence sprang Duret's theory of cerebrospinal fluid shock, which provided a theoretically good explanation of the reason why a blow on the vertex should injure the vital bulbar centres; and he, together with Koch and Filehne (1874) and especially Polis of Belgium and Miles of Edinburgh, published convincing experimental evidence that low-level disturbances even as caudal as the spinal cord (in which gross lesions were more often found than many remember) did

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actually occur. Gavin Miller (1927) repeated much of this work, and was able to cause concussion in the heartless frog as had Schiff, Goltz, and Witkowski before him. The problems were restated and retested by Denny-Brown and Ritchie Russell (1941) in a most important experimental series in which the evidences of brain-stem paralysis were proved to be well founded, with the entirely novel discovery that concussion could much more easily be produced if the head were free to move when it was struck. The essential factor was the suddenness of the acceleration imparted to the head and, in different circumstances, of the deceleration. The immediate alteration in respiratory rhythm, in pulse rate, blood pressure, pinna and corneal reflexes found by others, were again observed. A vital fact was that concussion could be produced without deformation of the skull—a rebuttal of the common surgical pictorial representation of indentation of the skull compressing the brain. None the less, the active cause remains a sudden application of energy to the brain. It is important to note that Denny-Brown and Russell had been able to produce concussion in decerebrate animals. These experimenters had nothing new to offer on the cause of the most impressive feature of concussion—unconsciousness itself—since their animals were either anaesthetized or decerebrate. We can safely leave the fundamentals of concussion other than this last as resting on a firm basis of experimental proof linked with clinical observation, and conclude that whatever alterations in cerebral blood supply either accompany or follow a concussive blow are secondary or epiphenomena, and that the prime cause is a paralytic effect on the neurons of which the brain mass is composed, including those of the brain-stem.

Unconsciousness or Traumatic Stupor

The question is, What part is played by the cerebral hemispheres, the cortex, and the deeper nuclei in the concussion or contusional syndrome? The majority of writers have assumed that consciousness is mediated by the cortex, and it will be immediately conceded that of full consciousness in the psychologist's sense this is certainly true. What is more, the occurrence of fits, often of focal type, the development of paralysis and of post-traumatic mental disorders, and the discoveries made at necropsy all certified that cortical and sub-cortical lesions of various degree and in various situations could sometimes, but not always, be found at high levels of neural integration and were not to be denied their importance in the total clinical picture. Are these the cause of stupor? The experiments of Tillman (1899) on the sliding movements between grey and white matter because of differences in their specific gravity, the cover-glass experiments of Ferrari in Kocher's laboratory, searches into the histology of the cortex after injury (Jacob, von Holder, 1904), all attest this concentration of inquiry on the cortex. More recently Greenfield (1938) demonstrated the demyelination that often follows severe injury. All these studies, save Greenfield's, ended without conclusions of a convincing kind, because the inquirers failed to realize what seems to be fundamental fact—that injury, that contusion, paralyzes nervous actions without the necessity for the effects of the contusion to be either macroscopically or microscopically visible, as was correctly stated by Trotter in his classical definition. The proof lies in the vigorous scrutiny of the facts of concussion itself and of contusion of the spinal cord and peripheral nerves. Laboratory work on the passage of impulses along axons (Erlanger) and on transmission at the synapse agrees that these are easily disturbed without gross alteration in structure. There is much that we must learn about the living conditions of the neuron, single or in vast communal partnership, after injury; physiological analysis by electrical methods holds out more hope of success than anatomical study. We should become better able through biophysics and micro-chemistry to demonstrate electro-chemical deviations from normal under injury.

Turning to clinical study of concussion or contusional cases, we are presented with material which is almost too rich, coloured as it is by individual differences of the patients' personalities and behavioural possibilities, and we are driven to the conclusion that there is no single fact or any group of facts which will tell us the course of unconsciousness in head injuries without confirmation from other sources. I have long believed that the classical stupor-recovery-stupor sequence

of intracranial bleeding might hold the key to the problem. I know now that it does so.

There can at this date be little doubt that traumatic stupor is produced by a low-level lesion—hypothalamic and brain-stem. Suggestions to that end have been made in the past by Heubel and by Breslau (1914) in favour of the fourth ventricle, Knauer and Enderlen (1922) for the mid-brain. Both Heubel and Witkowski found that when they opened the skull of a frog and touched the fourth ventricle with the head of a needle the animal, after showing evidence of pain, fell into a completely comatose condition lasting a longer or shorter time; the same result could be got in rabbits. Witkowski held that this condition closely resembled concussion. Breslau had witnessed the accidental injection of novocain through the foramen ovale into the posterior fossa in anaesthetizing the human trigeminal nerve—an act which produced stupor. On experiment he found that the injection of fluid into the posterior fossa of animals also had that effect. Something more than the tentative support to the doctrine of consciousness as a low-level affair has been adduced for non-traumatic causes by Penfield (1938) and by J. C. White (1940). In this country J. G. Greenfield also suggested it. Not only have animals been rendered unconscious by experimental injuries to the upper end of the fourth ventricle at pontine level but, what is more convincing, injuries inflicted on man on comparable areas, especially in attacks on acoustic neuromas, are usually attended, when fatal, by unconsciousness from the moment of operation. It is in fact one of the most striking of neurosurgical phenomena that unconsciousness can be so readily produced by disasters in the posterior fossa and that ventricular drainage, which reduces the hemispherical pressure to zero, has no effect in restoring consciousness though the dynamics of the cortical circulation and hemispherical tissue respiration must have been restored to normal. Nor does pressure of brief duration when generalized cause unconsciousness, as Browder in particular has shown in the human. I can support that observation. That it may do so in time none will deny, but then for the special reason that pressure sustained for some hours or days causes a prolapse of the temporal lobe on the compressed side (or of both lobes if the compressing agent is medial and more distant) into the tentorial hiatus. Here a cone is formed which compresses the diencephalon and rostral end of the mid-brain, and unless this can be relieved by the appropriate surgical measures unconsciousness will continue until autonomic breakdown causes death. This is the explanation of the fact that surgical mortality chiefly occurs in cases with unrelievable pressure cones or when bleeding into the mid-brain has already taken place. There is little doubt that a cone at this level is more frequent and more dangerous (because less easily relieved) than the better-known one at the level of the foramen magnum.

Focal Lesions causing Stupor

I have said that evidence on the localization of consciousness (and I shall shortly return to a statement of its nature) can be produced from other sources. Mention has been made of the fact that a posterior fossa lesion may cause unconsciousness. The notion that the stupor is caused by so severe a damming-back of the c.s.f. in the ventricles that cortical anaemia results is destroyed by the observation that the state may persist when intraventricular pressure is reduced to atmospheric. It is true that puncture may relieve, but the vital point is that it does not necessarily do so and that the patient may die with everything above the tentorium, or at least above the hypothalamus, apparently normal.

Clean-cut examples of brain-stem or hypothalamic lesions causing coma are presented by the following cases:

Case 1.—A. B., aged 48. Admitted Neurosurgical Service, Manchester Royal Infirmary. Referred by Dr. O. M. Duthie from the Royal Eye Hospital Dec. 10, 1942, on account of protrusion of right eye for 3½ months. The local signs are not important for the present discussion. A right-sided bone flap was turned down and the orbit unroofed, with the discovery of a small resistant mass in the midst of oedematous orbital contents. It was judged to be non-neoplastic, and the operation was concluded as an orbital decompression of the Naffziger type. The patient's pulse was rapid throughout the operation. She did not recover consciousness, and died 48 hours later in hyperthermia. Her pulse rate ranged between 174 and 152, with respirations in the 40s and 50s and a temperature that varied between 99.6° and 104° on the first day and between 102° and 105° on the

second. Occasionally she looked as if she might be about to wake up and half opened her eyes, giving the impression that she might be rousable and might speak if she could be sufficiently interested. All efforts to make contact failed and stupor returned.

The problem is, Why had this patient died? I suggested that a mid-brain or periventricular haemorrhage caused by anoxia in a long nitrous oxide anaesthesia might be the cause. However, at necropsy it was found (1) that the nodule in the orbit was a thrombosed aneurysm of the ophthalmic artery; (2) that there was no extradural clot; (3) that externally the brain was completely normal; (4) that she had died from the local compressive effects of the rupture of a second aneurysm in the cerebellar vermis with blood-clot plugging the iter (see Fig.).

This is a convincing example of the unconsciousness caused by a lesion at infra- and per-tentorial level; the fact that it caused death is less remarkable than its effect on total behaviour.

Case 2.—A woman aged 32 was referred by my medical colleague Dr. A. H. Holmes as a case of pituitary adenoma. What was unusual was the severity of her pain and the fact that she was drowsy and ill. Operation was performed and an unusually vascular chromophil adenoma cleared out easily. The patient failed to regain consciousness and died, much as did the previous case, in hyperthermia. Necropsy disclosed no contusion of the brain and an average small amount of subarachnoid blood in the basal cisterns. On section of the brain the cause of death was found to be a local clot some 3 cm. in diameter in a suprasellar situation occupying the third ventricle. Once more the essential fact is not that the patient died but that a localized clot in this situation caused stupor.

Case 3.—Mrs. G., aged 31, had the usual signs of a left-sided acoustic neuroma. It was evident from the neurological disturbances that this tumour was of very considerable size. At operation, Jan. 10, 1942, an exceedingly large tumour was subtotally removed, its complete extirpation proving to be impossible. During the manipulations her blood pressure rose to 180, the pulse falling to 60. Five hours after the operation she was moving her arms but would not rouse. She perspired freely and her face was flushed; there was a general vasomotor relaxation. The patient died in this condition 18 hours later with shallow rapid respirations and some evidence of pulmonary oedema. At necropsy the remains of the tumour were found to extend into the hiatus tentorii, and there were discrete haemorrhages in the mid-brain and pons. The cerebral hemispheres were in all respects normal.

In Cases 2 and 3, so far as could be observed, the cerebral hemispheres and the anterior hypothalamus were normal; although all the patients made movements they remained in

stupor. These cases demonstrate the prime importance to consciousness of intact integrative pathways in a vertical direction, and demonstrate also that anatomically undamaged connexions in and between the hemispheres themselves are not sufficient to maintain consciousness. This is in some ways a surprising conclusion, but there is no doubt of its truth. Other examples might easily be adduced, but for the moment these will suffice while we turn to the essential point—the nature of this stupor, this state that we call unconsciousness.

The Nature of Unconsciousness

The description of diseased or abnormal states by delineating them as the reverse of a defined normal is not one which has commended itself to medical science. This holds true of definitions of consciousness and unconsciousness. We might accept the statement that consciousness is a state in which man (or animals for that matter) respond to environment in a manner which shows insight (cf. Penfield and Erickson, 1941). It is true to say that unconsciousness and the stages of recovery from it, even when they are long-drawn-out, can be comprehended by the reverse of the foregoing—that the patient does not to this or that degree show insight into the problems which his environment sets from day by day or hour by hour; but the statement lacks the necessary crispness. It would be more helpful to define unconsciousness, whether traumatic or otherwise, by a new term which designated more pointedly its nature, its pathological status in terms of neurophysiology. When we watch a patient recovering from concussion we see him sleeping most of the day and night, disturbed at first by only the most intense stimuli, aroused not by thirst or hunger but principally by the pain of bladder distension, made restless by it and sometimes also by pains in the head or elsewhere which he does not understand, cannot analyse. As he recovers, sleep is less compulsive; insight into his state increases. Conversely, when we watch, as occasionally we must, a patient dropping into coma, the picture is even more clearly derived from sleep. At first susceptible to both internal and external stimuli, interest is lost in food, incontinence develops, until stage by stage the hypersomnic periods merge into complete negativism and an unrousability from which there is no reveille. Step by step alterations in pulse rate, thermal control, and water balance take place which culminate in metabolic disaster, local or general, and death.

Parasomnia

We approach closer to the facts of clinical observation if we speak of unnatural or, in the case of concussion, of traumatic sleep rather than of unconsciousness. Traumatic stupor is a better term than unconsciousness because it has for most of us a certain sleep connotation. There is an advantage in inventing a new term to overcome these difficulties. Something is needed with a sleep meaning but indicative of a condition different from ordinary sleep. The best that suggests itself to me is "parasomnia," a state in which there is no response to stimuli, verbal or mechanical, except those of a reflex nature. In other words, there is no response showing insight into or analysis of the problem set by the stimulus—at least no more than there is in a sleeping person. Variations in the picture can be regarded as the arrest of a moment of awakening and the giving to it of duration. This makes it a completely abnormal condition, and although we may for convenience regard it as an instantaneous freezing of a normal state, this must not blind us to the fact that it is pathological and associated with other abnormalities which further testify to that fact. Whatever words we use we should in future think in terms of sleep and wakefulness. The tossings, nose and body rubbings, mutterings, and unruliness occurring with some head injuries show that cortical actions continue, and compare with those observed by Kleitman (1939) in his studies of sleeping beings. And there is no doubt a high-level disturbance or inhibition of the cortex, partial or complete. But cortical lesions pure and simple do not seem to produce it, nor do massive excisions of the cerebral lobes, as I can well testify. No completely satisfactory human decortication is ever brought about by disease, and certainly never by surgery. We lack that piece of evidence. Yet a small central and basal injury certainly does so. This brings us, if the interpretation

which I have given is accepted, head on to the localization of the sleep centres variously placed in the anterior periventricular grey matter of the third ventricle or deeper in the posterior hypothalamus, in the anterior hypothalamus (meaning these areas plus some so far indefinable parts of the basal ganglia), or in the upper pons, or in all (von Economo, 1926, 1930; Fulton and Bailey, 1929; Ranson and Magoun, 1939; Globus, 1940; White, 1940). Nothing could be clearer than the fact that lesions in these areas have an effect on consciousness. Neurosurgery and neuropathology have done much to confirm the truth of observations made in the laboratory. And since lesions in these areas cause stupor and hypersomnia we cannot deny that trauma most probably produces its effects on consciousness in the same areas. It would be ingenuous to believe that there is a nucleus which controls sleep. The obtundation of consciousness must be a highly complex action in which the whole nervous system co-operates. It seems more logical to postulate a "waking centre" (and by "centre" I do not mean a cluster of cells but a circumscribed brain area, injury to or stimulation of which causes certain constant results), damage to which would result in hypersomnia, ending in that mixture of sleep and illness which I have just called parasomnia. Although the area of these waking centres is roughly known we cannot always demonstrate injuries in them. As Symonds pointed out, it is no more "required" to show histological changes than it is in post-epileptic stupor and in Todd's post-epileptic paralysis. Denny-Brown and Russell and their forerunners all showed that animals could be killed without verifiable alterations in nervous structure. But it is a fact that mid-brain, hypothalamic, and pontine lesions can be demonstrated in some persons who die from injury as well as in those who die from tumours. The limits of the region concerned have still to be accurately mapped. Disturbances of the lower closed part of the medulla oblongata seem to be less able to disturb consciousness than those in the upper half of the fourth ventricle, but even that is unsure. The rostral extent is even more difficult to give with precision; it might extend into the palaeocerebrum wide of the third ventricle.

It would be a valuable step if we knew the behaviour not only of a single cell under trauma but of many cells, their rate and regularity of firing, the "boosting" required, the changes that occurred in cell respiration, and enzyme requirements. Further, we shall need to know the effects of trauma on electrical potentials and fibre transmission at different levels of the brain from the cortex to the cord and, if possible, at all levels at the same time. A valuable start was made by Dennis Williams and Denny-Brown (1941) and is being further elaborated by Earl Walker. The e.e.g. pattern is often very similar in sleep to that seen after concussion; there is the same disappearance of fast activity and the same appearance of high-voltage slow waves. As for the circulatory disturbances after head injury, there is a good deal of evidence that these happen in the severer cases. But whether they are occasioned by the stretching of the vessel walls by the agency of the momentary compression of contained blood, or whether they are the result of disturbance of a vasomotor centre or centres or arise from altered oxygen and carbon dioxide tensions, we have still to learn. The experiments of White show that there is a slight increase in brain mass after an injury, but oedema of a severe grade seems to be limited to the periphery of areas of actual contusion (Greenfield). We have to regard cerebral pathology after injury as a moving picture altering from day to day. Beyond a certain point there may be a progressive break-up of integration that must eventually be measurable in terms of cell metabolism as well as the transmission of impulses. Some petechial haemorrhages certainly arise secondarily, and are not the immediate effects of the violence. Changes in the vessel walls are visible within a few hours after injury, and these must effect the filtration of plasma elements and finally even of erythrocytes.

If we agree that the major phenomena produced by concussion are not primarily cortical, and are usually recovered from because in the majority of cases the disturbance is a physiological one without gross and persistent underlying alteration in structure, we can more properly understand that the results should so often be good and may be less inclined to accept easily a pessimistic view in prognosis.

Cortical Activities

The foregoing account has but lightly touched on the activities of the cortex in concussion, and maybe their importance has been unduly minimized. We know of them chiefly from psychological study and from e.e.g. analysis—two methods which are only in process of correlation. Reference has been made to the effect of a mid-brain lesion in interrupting integrative impulses in caudal and rostral directions and the profound effect that such a block seems to have on what might have been regarded as largely intercortical activities. These facts are fully in accord with Kleitman's views on the nature of sleep. A similar conception underlies the state of akinetic mutism described by Cairns, Oldfield, Pennybacker, and Whitteridge (1941). This again is a negative state affecting both intellectual and emotional tone, and in the one well-described case on which their paper depends its basis in a third ventricle lesion was well attested. Observations incline me to believe that parasomnia and akinetic mutism are not the same thing, but that many patients with cerebral contusion or with tumours can go through this mute state on the way to recovery or, conversely, towards coma. Speed of change may prevent its detection or development as a definable condition. For example, in two of the clinical cases recorded above there were moments when the state resembled akinetic mutism alternating with restlessness and mutism and parasomnia. The difference lies in the sleep propensities of the states; it is the dominant factor in the one, not so in the other. Nor does it seem probable that akinetic mutism is any more to be separated from general physical disorder than is parasomnia. It must be made clear that I do not regard the latter as a purely mental state; it is something more total than that. The recognition of these two states, if further observation by others confirms their validity, would mark a step in the unravelling of behavioural peculiarities at a lower level of psychological functioning than has so far been freely explored.

The long-lasting mental confusion, the Korsakov syndromes, the patchy or incoherent memory, which persist for many days or even weeks after some severe head injuries, can only be explained by disturbances of total brain functions which might, though not certainly, be due purely to cortical blocks. How far they derive from actual anatomical alteration we do not know. Common sense seems to say that they must have such dependence, but a certain amount of agnosticism is allowable. Occasionally the post-traumatic mental state resembles that seen after bromide intoxication and no doubt from other toxic agents. We do not yet know for how long the interactions of neuronal constellations may be disordered without actual damage in the sense in which we mean it at present. Perhaps, in the future, advances in the technique of recording action potentials will reveal abnormalities in the quality, quantity, and timing of cell discharges and axonal conduction, with a chemical or enzyme background of abnormality induced by the injury, disturbing the co-ordination of those "self-mending electrical leaks" (as Sherrington calls them) that underlie neural activities. Only in some such manner can one postulate a cause for that Jacksonian dissolution of nervous integration that signifies in different ways, at different stages, the nature of concussion. We suspect, though it is not yet proved, that general cerebral contusion causes a disturbance in the cerebral blood supply which may conduce to abnormality without necessarily originating it.

Trauma as a Disease Process

In conclusion, no statement on concussion would be complete without mention of a matter which has so far attracted no comment—the cause of death in those who survive the immediate injury. Necropsy material is insufficiently explanatory because we are dealing with a functional disorder. Explanation has run into wrong channels through the belief that abnormalities of action must always be accompanied by gross change (and in that term I include microscopy). The discovery of cortical injury (though much less than the surgeon can inflict with impunity), the finding of subarachnoid haemorrhage (though no more in amount than many with leaking aneurysms survive), the presence of relatively small quantities of subdural blood, are not enough to account for death, though

I should be the last to deny that all of these things can cause death when they are severe enough. But it must be strongly asserted that the findings in human beings are often disappointingly small—disappointing, that is, to the mind which is prepared only for anatomical findings. Yet it is not these things, nor the petechial haemorrhages of classical times, which tell us most; it is rather their variability or their absence. To find nothing would be in line with the most informative of experimental evidence. This raises the question as to how it can come about that an initial lesion severe enough to cause neural paralysis can be survived though death occurs hours or days afterwards. There is no question about the fact that this can and does happen; and it is certain, it is sure. Only one explanation suggests itself—that an injury sets going a self-propagating event that leads sooner or later to death. It would be a mistake to draw too much on analogy, and any explanation must be regarded as both speculative and tentative. But death from burns, from fractures, and from haemorrhages will serve as shorthand notes indicating at least a parallelism. We can only speculate at the moment on what the answer will be in the case of cerebral contusion. It is the fate of all of us to watch patients with cerebral lesions dying from something characterized by tachycardia and cardiac irregularity, from upsets of thermal regulation, from metabolic disturbance which we have not yet found a means to study properly, from something that bears the hall-mark of a disease process as much as, say, pneumonia. The old beliefs in the omnipotence of the bulbar centres has been corrected by the discovery of the vital centres re-representing them at and above the tentorial level. Conceivably it may become possible to demonstrate alteration in oxidation-reduction mechanisms in this area which will afford an index of cellular pathology. It seems legitimate to suppose that the physical effects of injury lead to affection of at least one enzyme system, the lack of which can for a time be repaired by the altered energies of others, which also in turn give out. Thus, step by step, dissolution comes about. Only in such a way can temporary survival with final extinction be given a cause. And it will be recognized that the level at which all of these happenings occur is in the more primitive but still no doubt extremely complex and largely integrated neural mechanisms considerably below cortical level.

Conclusion

Although the beliefs expressed above have minimized the importance of the cortex in the picture of concussion, it is not my belief that cortical disturbances are absent. Electrical records clearly show that they are frequent; while some patients, by confusion, confabulation, and lack of insight (sometimes for many days after return to consciousness), demonstrate that the whole brain integration continues to be disturbed. It is not possible at the moment to do more than speculate on the causes and mechanisms of this dysfunction. The real point that I have wished to examine is the nature of unconsciousness, and I have endeavoured to show that there is a body of evidence attesting to its production in a relatively focal manner, and that the focus is not, as has been so generally believed, in the cerebral cortex.

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NUTRITIONAL DEFICIENCY IN THE PATHO-GENESIS OF DISEASE*

BY

JOHN YUDKIN, M.A., M.D., Ph.D., F.I.C.

Lieut. R.A.M.C.; formerly Sir Halley Stewart Research Fellow at Dunn Nutritional Laboratory, Medical Research Council and University of Cambridge

More and more has the role of vitamin deficiency claimed our attention in recent years, and a variety of diseases and syndromes have been treated with a vitamin or a combination of vitamins. Frequently the reasons for doing this are obscure and the results of the treatment equivocal; and the relation between the condition and vitamin deficiency often remains difficult to assess.

Nutritional deficiency may be responsible for the production either of a recognized disease, of hitherto unknown aetiology, or of obscure signs and symptoms in an individual. For example, claims are sometimes made that vitamin deficiency plays a part in the production of renal lithiasis (Higgins, 1935) and certain muscular dystrophies (Bicknell, 1940). Again, a patient is seen with an unusual form of keratosis of the skin, or with oedema which does not easily respond to ordinary therapy, or with a sore tongue with few other signs or symptoms, or with an unusual type of subcutaneous haemorrhage: to what extent are vitamin A, vitamin B₁, riboflavin, and vitamin C respectively implicated in the production of these disturbances in the individual?

In this paper I shall consider certain general principles which might act as a guide in the evaluation of the part played by vitamins in the causation of disease. Just as we use Koch's postulates in determining the role of specific bacteria in causing disease, so we may lay down the following criteria for assessing the role of nutritional deficiency in causing disease: (1) It should be possible to demonstrate the existence of a deficiency of the nutrient; (2) deficiency of the nutrient should result in the production of the disease; (3) the disease should be cured by replacement of the deficient nutrient. To satisfy each of these criteria,* evidence may be collected in several ways:

Diagnosis of Nutritional Deficiency

Criterion 1.—Existence of deficiency

A. General evidence of deficiency

- (i) Evidence of inadequate diet
- (ii) Evidence of defective absorption
- (iii) Evidence of increased utilization

B. Specific evidence of deficiency

- (i) Laboratory tests for specific deficiency
- (ii) Clinical tests for specific deficiency

Criterion 2.—Deficiency as the cause of the condition

- A. Evidence from animals
- B. Evidence from human beings

Criterion 3.—Cure of condition by correction of the deficiency

Therapeutic test

Criterion 1: Existence of Deficiency

The first criterion is that there should be evidence of nutritional deficiency in the condition. This evidence may be either general or specific.

A. General Evidence of Deficiency

There may be evidence of a deficiency in any part of the pathway between the nutrient and the tissues.

(i) Evidence of Inadequate Diet

A dietary history is an essential first step in diagnosis. The following conditions are especially apt to lead to an inadequate diet.

(a) *Low Income Levels.*—On the whole, foods which are good sources of vitamins are also more expensive; cheaper foods supply mainly calories (Orr, 1936).

(b) *War.*—Wartime measures, such as the introduction of the national loaf and the vitaminization of margarine, together with rationing, the price control of foods, and the distribution of cheap or free milk and fruit juices, have decreased the disparity between the diets of various classes. Nevertheless, there are many who still

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† Certain exceptions to the fulfilment of these criteria are discussed below.