The Dynamics of Brain Mechanisms in Neurological Dysfunction During Flying

Air Marshal Subroto Mukerjee Memorial Oration

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AIR Marshal Subroto Mukerjee, due to his unfailing interest and foresight, established medical service to cater to the needs of the Air Force. Due to his patronage and support the well-known National Institute of Aviation Medicine, the first of its kind in Asia came to be founded. Indeed his humanism and his sincere interest in the health and happiness of all ranks made him a pioneer in the field of maintaining high efficiency of the air wing of the Armed Forces. I consider it a rare privilege for me to be honoured to deliver the VIth Air Marshal Subroto Mukerjee Oration.

For over a decade that I have been a honorary consultant to the Armed Forces, the problems which frequently came for scrutiny were the health difficulties of trained pilots who sometimes during flight had a black out or a fit. Decision had to be taken as to the flying fitness of these officers. Quite often it had not been an easy task and even when the final conclusion was arrived at, a lurking doubt remained as to whether it was a decision without any flaw. This was the dilemma which lead me to go into the various aspects of this episodic illness which could be catastrophic. The magnitude of this proposition has been adequately discussed in two recent publications (1-3). In this oration I shall deal with—" The dynamics of brain mechanisms in neurological dysfunction during flying".

A lot of important advances have been made and the concept of compartmentation in the brain (Waelsch 1961; Tower et al, 1961) has been very helpful to clarify the understanding of brain functions under stress. There are intra and intercompartmental dynamics which operate and determine the safety or otherwise of the nervous system when it negotiates the flight emergencies.

These compartments consists of :—

(*i*) Vascular compartment

(*ii*) Cerebrospinal fluid and extracellular space compartment, and

(*iii*) Cellular compartment in which the metabolism of neurons and neuroglial cells is involved.

Although in classification these compartments are segregated but in function they are so closely dependent and correlated to each other that they operate as one unit and any change in the adjustment of one necessarily lead to a corresponding adaptive change in the other two. Thus functional efficiency and a proper homeostasis of the melieu interior in these compartments is well looked after.

The Vascular compartment

This consists of—

(*a*) the big vessels at the base of the brain all lying in the subarachnoid space,

(*b*) the arterioles which penetrate the brain substance leading to,

(*c*) the intercerebral capillary system both arterial and venous and,

(*d*) the venous sinuses and veins lying on the surface of the brain.

Each one of these segments of the total vasculature which participate in the autoregulation of

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brain circulation has some special features which act as safety measures during the acceleration stresses of flight. Failure at any stage leads to such emergencies as black outs and fits leading to unconsciousness or coma.

(*a*) The big vessels at the base of the brain lying in the subarachnoid space—Recent demonstration of chordae system by the Russian workers (Aruthiunovx et at, 1974) has greatly facilitated to understand some of the problems of cerebral circulation in acceleration and deceleration. These chordes are fibroelastic structures which have various types of relationship in their attachment to the vessels and the lining of the subcrachnoid space.

Type I chordae: They stabilise the position of an artery with reference to the wall of the C.S.F. pathway in which the artery lies. A cross section of the C.S.F. channel with an artery located in it shows these chordae clearly. They suspend the artery from the walls of the C.S:F. channel. One end of the chordae is interlaced in the arterial adventitia and the other end is fixed to the wall of the channel. A variation of this type sometimes form a kind of hammock in which the artery rests, both ends of chordae being fixed to the walls of the C.S. F. channel. Another variety which characteristically is present for the posterior inferior cerebellar-artery has the form of brackets consisting of short and interanastomosing fibrils binding the vessel to the surface of the cerebellum.

Type II chordae: They operate to keep the configuration of the loop or bend of a vessel in a stabilised state without too much of an alteration in its shape. These chordae are like bowstrings with auxiliary fixation points on the concave side of the artery. Apparently they allow the shape of the curve to change only within certain limits.

Type III chordae: This variety serves the purpose of keeping the branches of an artery in a certain relationship with the parent vessel without too much variation in the positional relationship. They often are in the form of a rein with a loop at one end through which the branch of the artery passes.

The three types of chordae with a thickness varying from 25 μ to 200 μ are abundantly present in vessels as far as the point where they dip into the cerebral cortex. They are however completely absent in so far as the veins are concerned.

Their normal function is that they control the position of the arteries in relation to the walls of the C.S.F. pathway at the base of the brain and upto the cerebral cortex.

They limit physical deformation due to arterial pulsation or respiratory displacements. They are effective agents in preventing displacement and deformation of arteries during acceleratory or decceleratory stress and thus prevent any changes in circulation which may sometimes produce blackouts and syncope. Such sudden alterations in circulatory dynamics often are far beyond the range of autoregulation mechanism to cope with. This has been demonstrated in monkeys by giving 4 meter per second impact transversely at tempro-parietal and occipital regions and doing high speed angiography (Shatsky, 1974). It has been seen that this type of acceleration produces ipsilateral transitory-displacement of anterior and middle cerebral arteries when force is applied to tempro-parietal region and middle cerebral and posterior cerebral arteries with occipital region impact. There are also similar displacements that are momentary and are corrected within a very short time.

There is one more function attributed to those chordae. They not only act mechanically but also contain in them neuronal elements which operate to give rise to segmental constriction of a vessel thereby controlling an abnormal surge or deficiency of blood flow. These neuronal elements are present in the form of one or more ganglion cells which send their axons to end on the vasculature of the artery. They are regional and localised structures but some of them receive sympathetic fibres from the superior cervical sympathetic ganglion which sends sympathetic fibres along the carotid and vertebral arteries.

(*b*) Arterioles which penetrate the brain substance: These continue to subdivide till they form the terminal and meta-arterioles which have considerable reduction in the muscular layer. Except for the initial arterioles near the pial surface which are supplied by the same sympathetic supply which innervates the big vessels outside

the cerebral tissues, the terminal and meta-arteriols get their innervation from the ascending axons which belong to neurons situated in the brain stem forming the central autonomic system. Electronmicroscopically it has been shown (Cervos-Navarro and Malakis, 1975; Raichel et al, 1975 and Renols and Nelson, 1975) that the muscular walls of the terminal and meta-arterioles have on them axon terminals containing vesicles of neuro-transmitters. Also stimulation of certain localized neuronal pools in the brain stem sterotaxically leads to either vasoconstriction or vasodilatation of these vessels (Meyer et al 1971). It is easy to surmise from these findings that any transitory acceleratory force which produces reversible displacement of brain stem can easily produce wide-spread vasoconstriction or dilatation of intracerebral blood vessels which due to changes in blood flow affect pH and gasseous exchange of CO_2 and O_2 precipitating evanescent or more lasting symptomatology of black outs, fits and syncope.

(c) Intracerebral capillary system (Zweifnel 1961) starts where the arteriolar system ends. These vessels have a well developed endothelial lining without pores but with distinct tight junctions, a thick basement membrane containing scattered pericytes and a well defined covering of astrocytic footplates. This entire structure complex is called the blood brain barrier. Quite often in this capillary bed there are also seen thoroughfare vessels associated with a bunch of capillaries around them. There are also demonstrated some narrow sphincter like structures at the site of angular branching off of capillaries arising from the arterioles. In capillary beds in which thoroughfare vessels are present, most of the time the blood flows in these vessels rather than through the whole capillary bed. Also when the sphincters at the bifurcation function, they block the entry of RBC but allow the plasma to circulate through the capillaries intermittently. This capillary system has the same type of nerve supply from the brain stem as on the arterioles but here it controls the permeability rather than the contractility.

This very extensive vasuclar bed is the chief site of autoregulation of cerebral circulation which on one side is influenced by blood flow in the big extra-cerebral arteries and intracerebral arterioles and on the other side by the functional state of the venous system fed by the capillary bed.

This is the region in which circulatory change are by and large regulated by the local biochemical melieu i.e. PH, CO_2 and oxygen content, bioamines and other vasoactive substances contained in the surrounding interstitial fluid and the C.S.F. compartments.

Under influences of strain and stress due to G forces during acceleration and deceleration producing circulatory and biochemical changes, the permeability of the vast vesecular bed is effected leading to leakage from the vessels ending in cerebral oedema of varying degrees. This may be reversible or irreversible. Whether the oedema is due more to intracellular or extracellular fluid retention, depends on the degree of anoxia or the failure of autoregulation, therefore the former leading to intracellular and the latter to extracellular fluid retention.

This diffuse but irregular pathological change produces symptoms such as acute headaches, giddiness, unconsciousness of various grade with focal or generalized fits. Quite often there are seen associated changes in the fundus and other systemic symptoms involving respiratory and circulatory systems.

Cerebrospinal fluid and the extracellular space compartment.

This system is also called the 3rd circulation (Milhorat 1975). The cerebrospinal fluid is formed 60% by choroid plexus and the rest of 40% is formed in the brain substance at the blood brain barrier level, or by the astrocytes. The former chiefly is contained in the ventricular system and the latter in the extracellular space of the brain substance. There is however a free mixing up of the C.S.F. flowing in the two types of spaces, eg: ventricular and extracellular space, either through the ependymal lining or by an active transport system in the astroglial cells by dint of their processes which end on the lining of the subarachnoid space. The concept of formation of C.S.F. in the brain substance to the extent of 40% of the total has greatly helped to understand some of the pathological changes as extracellular oedema of the brain under effect of D. forces. These forces seem to disturb the permeability at the blood brain barrier sites or the function of astrocytes or both. Essentially these effects are brought about by altered

circulatory dynamics in the vascular compartment which consequently changes the 02 supply, the C02 tension and pH variations.

Cellular compartment

Cellular compartment consists mainly of neurones the neuroglial cells and the intracellular and extracellular fluid contents. Metabolic changes produced in these cells due to flying stresses mentioned already lead to circulatory changes and changes in the composition and dynamics of cerebrospinal fluid and the fluid in the extracellular spaces. It may be emphasised here that composition and movements of the extracellular fluid which forms the immediate environment of the nerve and glial cells has important morphological characteristics which determine the specificity of function of these cells.

Ontogenitically these spaces are wide in infancy and form intercommunicating network (pysh. 1963) in which the fluid medium has a wide and uniform effect on the dynamic cell biochemistry. As the cells multiply the intercellular space not only becomes narrow but also shows differentiation such as to segregate pools of cells which have a common functional activity. Such islets usually have a narrow outlet which establishes communication with the adjacent pool. In this way the intercellular space has extensive communication in general but it also is compartmentalized for the individual cell aggregations which are differentiated in their specific function.

Any derangement in fluid flow in these channels influences the specific metabolic and electrical functions of the cell colonies leading to a variety of symptomatology depending upon the particular function of the region. This effect may be focal when the damage is limited but is more diffuse when there is extensive oedema involving large parts of the brain. The metabolic changes are complicated involving the substrate, enzymes, and also electrolytes in the cell soma and synapsics but essentially they are brought about by hypoxia, hypo or hypercarbia and pH changes consequent to the circulatory changes of blood, of C. S. F. and extracellular fluid.

It is well known that respiratory alkalosis (Cervos-Navaro et al, 1971) due to hyperventilation frequently leads to marked increase of blood flow in the white matter and electronmicroscopically there is oedematous swelling of astrocytes. This is associated quite often with decrease of micropinocytoses. In acidosis due to hypoventilation on the other hand there is decompensation of cortical blood flow as the time passes by and the electron-microscopic picture mainly shows the clumping and diminution in number of synaptic vesicles. Astrocytes do not show any structural change.

Whenever changes in neuroglial tissue occur it invariably is associated with accumulation of glycogen in these cells. This has been proved experimentally to be due to oxygen deficiency and increased permeability of the blood brain barrier which is vasogenic and not cytotoxic in nature (Klatzo, 1971). The preferential site of damage is the white matter and the oedema fluid is rich in sodium chloride and proteins. This is different to 1) cytotoxic oedema in which grey matter is the primary target of change or 2) brain inflation in which there is dramatic increase in brain volume due to vascular dilation and dilatation of the ventricular system. It is commonly seen in diencephalic injuries. Once the cerebral oedema develops, it can by its own dynamics (Langfitt, 1971; Nils Lundberg, 1971) start a chain of events which often leads to irreversible damage. At first the C.S.F. space diminishes and subsequently due to compression of venous channels there is sudden increase in cerebral blood volume. Thus the intracranial pressure homeostasis is seriously threatened and if the therapeutical relief is not available herniation or coning of brain stem is inevitable which by its vasomotor effects further aggravates the brain damage.

The injury to the cellular population in oedematous cortex has concommitant effects on the energy metabolism of the cells (Reulen et al, 1971). There is however no uniformity of chemical reactions in all regions of the brain. Whilst some cellular aggregates show a more advanced metabolic changes, the others are comparatively less effected. The main biochemical defect noticeable is a marked diminution of creatine phosphate and ATP, with a consequent increase in ADP and AMP. Glucose shows diminution whilst lactic acid is significantly increased.

If the brain damage does not prove fatal and the patient pulls through the acute phase, clinical course of the illness is not identical in all cases. If it continues to be a protracted loss of consciousness,

the prognostic significance is sometimes fairly well surmised from the EEG changes. An unchanging monotonous rhythm of high voltage or low voltage slow waves indicate that the situation is serious and irreversible. If in 24 hours recording the EEG activity shows changes in frequency of voltage which further fluctuates from day to day, it is an indication of better prognosis (Tandon et al, 1976). It is especially true if slow sleep and REM phases are distinctly distinguishable. However even in these cases long range effects are unpredicable.

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