Matters arising

Phenylacetic acid in human body fluids

SIR: In the short report by Prof Sandler and his colleagues on phenylacetic acid in human body fluids (J. Neurol. Neurosurg. Psychiatry 1982;45:366–8), the authors question the general consensus that phenylacetic acid production mirrors that of endogenous phenylethylamine.

Investigations on myself and patients with cystic fibrosis indicate that a significant proportion of urinary phenylacetylglutamine (PAG) is derived from bacterial gut metabolism presumably phenylalanine released by bacterial proteolysis of unabsorbed protein residues. Thus replacement of all natural protein with an enzymatic hydrolyase of lacalumenum resulted in a reduction in the excretion of PAG to one fifth of the baseline value. In one patient with cystic fibrosis the replacement of natural protein by an equivalent L-amino acid mixture the excretion of PAG fell by 50%.

Phenylacetic acid or phenylethylamine formed in the large bowel and absorbed would be completely converted to phenylacetylglutamine on passing through the liver. Free phenylacetic acid in plasma rather than total or conjugated phenylacetic acid should, therefore, give a measure of the production of endogenous phenylethylamine.

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Cellular hypersensitivity to ionising radiation in Friedreich's ataxia

SIR: Robbins and his colleagues have since 1978 advocated an hypothesis that: (1) DNA repair is required to maintain the functional integrity of tissues composed of post-mitotic excitable cells such as the nervous system, retina, and skeletal muscle; (2) defective repair of DNA damaged in vivo by endogenous chemicals causes premature death of post-mitotic excitable cells such as neurons, retinal rods and cones, or skeletal muscle fibres; and (3) cells from patients with some diseases characterised by progressive neuronal degeneration, retinal degeneration, or muscular degeneration will be hypersensitive to DNA-damaging agents. Based upon this Robbins hypothesis, a new category of these neurological diseases characterised by abnormal hypersensitivity to DNA-damaging agents would include a number of disorders with widely varying symptomatology. In fibroblast or lymphoblast cultures, reproducible abnormalities can be demonstrated using either x-rays or the radiomimetic chemical N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) as the DNA-damaging agent. Diseases already determined to fit in the new category include ataxia telangectasia, Huntington's disease, familial dysautonomia (Riley-Day syndrome), Alzheimer's disease, Usher syndrome, and Parkinson's disease.

With their report in the Journal of Neurology, Neurosurgery and Psychiatry (1982; 45:1136–8), Chamberlain and Lewis added another disorder, Friedreich's ataxia, to the Robbins category of neurological diseases with hypersensitivity to DNA-damaging agents. Studies of these disorders can now be undertaken using readily accessible tissues for culture to determine the molecular basis for the hypersensitivity to DNA-damaging agents and to develop specific therapies. In addition, screening of carriers and pre-natal diagnosis may become practical in the future.

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Ruptured intracranial aneurysms

SIR: While it is not our intention to be involved in a prolonged communication, we cannot allow Mr. Maurice-Williams's (J. Neurol. Neurosurg. Psychiatry 1983;46:366) to misquote a paper from this unit. In that paper the following observations were made. The fall in mean cerebral blood flow (CBF) after a subarachnoid haemorrhage (SAH) with advancing age was not affected by patients taking tranexamic acid, that is, older patients had the lowest CBF irrespective of drug therapy. A progressive fall in CBF was noted during the first week after a SAH, a trend observed in both patients on and off drug therapy (adrenergic blockade and tranexamic acid). In all patients, regardless of drug treatment, a very low CBF was linked with a poor clinical outcome. This paper does not address itself to the effect of tranexamic acid on the CBF over a prolonged period in patients following a SAH. We would refer Mr. Maurice-Williams to another paper from this unit in which tranexamic acid produced a significant fall in CBF over a three week period following a SAH.

G NEIL-DWYER
MM SHARR

References


8 Scudiero DA, Meyer SA, Clutterback BE, Wirtschafter JD, Tarone RE, Robbins JH. Hypersensitivity to N-methyl-N'-nitro-N-nitrosoguanidine in fibroblasts from patients with pigmentary retinal degenera-


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References

Maurice-Williams replies:
I have carefully re-read the article concerned and I cannot see that I have misquoted it in my previous comment on the letter of Mr Scharr and Mr Neil-Dwyer. The subsequently published article does indeed report that administration of tranexamic acid appears to be associated with a fall in cerebral blood flow during the second week after subarachnoid haemorrhage. If this is confirmed it will clearly have very important implications with regard to the effect of anti-fibrinolytic drugs on patients with ruptured aneurysms. However it does not resolve the main point that I had hoped to get across in the paper that is the subject of this discussion—namely the differing time courses of confirmed re-bleeds and episodes of non-haemorrhagic deterioration and the fact that the time course of the latter coincides with the time course of rebleeding as reported in earlier studies, suggesting that those studies may have confused these two events and thus significantly overestimated the incidence of early rebleeding.

Notices

The Commonwealth Association for Mental Handicap and Developmental Disabilities (CAMHDD) has recently been formed with the support of a launching grant from the Commonwealth Foundation and has as its principal aims the prevention and amelioration of mental handicap and related developmental disabilities in developing Commonwealth countries. It is hoped that its membership ultimately will be that of individual professional and non-professional workers either working within developing countries in the field of mental handicap or those in developed countries that have a particular interest in this field in such countries. It is hoped to establish ultimately a form of directory of interested workers and from time to time practically orientated workshops will be held in differing developing countries. Further details may be obtained from the Association's UK Representative: Dr Gwilym Hosking, Consultant Paediatric Neurologist, The Ryegate Centre, Children's Hospital, Sheffield S10 5DD, UK.

Correction


The authors wish to correct the figures in the last column of table 1, where the values for "Neurologists/100,000 population" were too high by a factor of 100. Thus, for example, the figure for London should have been 1.15, for Greater Manchester 0.30.