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 fibrosis¹ 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 enzymic hydrolysate of lacalbumen 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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Reference

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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.¹⁻⁴ Based upon this Robbins hypothesis, a proposed 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 telangiectasia, Huntington's disease, familial dysautonomia (Riley-Day syndrome), Alzheimer's disease, Usher syndrome, and Parkinson's disease.⁵⁻¹⁰ With their report in the Journal of Neurology, Neurosurgery and Psychiatry (1982; 45:1136-8), Chamberlain and Lewis add 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 (Neurology, Neurosurgery and Psychiatry 1983;46:366) to misquote a paper from this unit.¹ In that paper the following observations were made. The fall in mean cerebral blood flow (MCBF) 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 unit² in which tranexamic acid produced a significant fall in CBF over a three week period following a SAH.

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