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 degeneration, retinal degeneration, or muscular degeneration will be hypersensitive to DNA-damaging agents. 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 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, Friedrich'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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Reference


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 proposed new category of these neurological diseases characterised by abnormal hypersensitivity to DNA-damaging agents would include a number of disorders with widely varying symptomology. 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, Friedrich'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 report (Brain 1983;106:366) to misquote a paper from this unit. In that paper the following observations were made. The fall in mean cerebral blood flow (MBF) after a subarachnoid haemorrhage (SAH) with advancing age was not affected by patients taking tranexamic acid, that is, older patients had the lowest MBF irrespective of drug therapy. A progressive fall in MBF 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 MBF was linked with a poor clinical outcome. This paper does not address itself to the effect of tranexamic acid on the MBF 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 MBF over a three week period following a SAH.

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References