Matters arising

Papilloedema with extramedullary erythropoiesis and Cushing's syndrome.

Sir: It is possible that the severe papilloedema which appeared after the use of metapyrone in the patient described by Griffith and colleagues was caused by a sudden reduction in circulating levels of cortisol.

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References


Griffith replies:
Dr Neville makes a reasonable point but we are grateful for the opportunity to present further information which makes this suggestion appear unlikely to be the correct explanation. Not only was the patient commenced on hydrocortisone (30 mg/day) at the time of starting metapyrone, thus preventing a hypocortisolaemic state in absolute terms, but neither was a rapid fall in cortisol levels induced as no overall reduction had been caused by the metapyrone when papilloedema developed, as shown by the following values:

Metapyrone was commenced on 22nd September and papilloedema noted on 7th October.

Plasma cortisols (nmol/L) - 9.00 a.m. values:
6th August 630
25th September 925
3rd October 605

Midnight values:
4th August 775
25th September 640
2nd October 950

Urinary free cortisols (nmol/24 hours) (Normal range 220-1030)
19th September 4550
4th October 9255.

Syringomyelia, an hypothesis and proposed method of treatment

Sir: I have hesitated to reply to Mr Williams' comment on my views about syringomyelia (J Neurol Neurosurg Psychiatry 1983;46:365-7), because of my respect for his great knowledge, originality and expertise in the matter, in case it appears that I am in controversy with him. In fact, I think our views are complementary.

I have described the wedge and Mr Williams has described the hammer.

I suggested that the reason that the syrinx in the spinal cord continued to extend at its ends, was that it had an oval shape imposed upon it by the covering of the spinal cord and longitudinal arrangement of its tissue planes. The ends of the syrinx were the sites of maximal stress in the capsule in accordance with well understood physical laws (that is, that the tension in the wall, \( T \), of a cavity is inversely proportional to the sum of reciprocals of the principal radii of curvature of the wall, \( R_1 \) and \( R_2 \), and proportional to the pressure difference \( \Delta P \) across the wall).

\[
T = \Delta P \left( \frac{1}{R_1} + \frac{1}{R_2} \right)
\]

That is, where the curvature is greatest, so is the tension in the walls, and hence a cavity is most likely to rupture its capsule at its sharpest point—this is in accord with everyday experience, and Laplace's theorem is a special case of this general formula.

The phenomenon of syringomyelia occurs only in the spinal cord because in other areas of the central nervous system, cavities tend to assume a more spherical shape in compliance with these same laws. In a sphere the tension is evenly distributed over the whole wall so there is no point of excessive tension where rupture is likely. It is similar to the situation of a bubble which assumes a spherical shape as this is the only stable shape. In the spinal cord, however, the covering and tissue planes prevent the formation of a sphere and a cavity assumes an ovoid shape with relatively sharp ends. Hence the shape and mechanics of the syrinx necessarily form a potential fluid wedge in the spinal cord.

Mr Williams' careful work has described how cough impulses and other causes of a rise in CSF pressure may produce a hammer which drives the wedge along the cord. The rises of pressure in the fluid of the syrinx, whether open or closed, will produce stresses in the wall of the syrinx which will be most likely to rupture it at the sharp ends of the syrinx.

Thus, the two views are not incompatible but complementary. The structure of the spinal cord makes any fluid filled cavity, open or closed, ovoid and thus a potential wedge which may be hammered along the grain of the spinal cord by those sudden rises in pressure which Mr Williams has demonstrated with coughing or Valsalva's manoeuvres.

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Sir: Edwards and Glen-Bott (J Neurol, Neurosurg, Psychiatry 1984;47:960-4) considered the potential of vloxazine to precipitate seizures in patients, and concentrate on the evidence from the Committee of Safety of Medicines (CSM). They correctly note that this compound is generally thought to have less epileptogenic properties than many other antidepressants, but in their summary conclude with the statement that this drug "is not contraindicated in epileptic patients requiring antidepressant medication".

Although the seizurogenic properties of antidepressants are clearly important when prescribing psychotropic drugs to epileptic patients, another important factor considered by Edwards and Glen-Bott only in the very last line of their article is the pharmacokinetic interaction between the antidepressants and the anticonvulsants. Although there are few investigations of this subject there is now growing evidence that vloxazine may interact adversely with several commonly used anticonvulsant preparations. Thus, early trials provided some evidence that vloxazine may precipitate phenytoin intoxication and more recent data reported by Pisani et al refer to an interaction with carbamazepine. In the latter study, five out of seven patients developed symptoms of carbamazepine intoxication following the administration of vloxazine, and discontinuation of the antidepressant resulted in remission of symptoms, suggestive of toxicity, and a return of elevated serum carbamazepine levels to acceptable values. In one patient vloxazine was associated with a rise in phenobarbitone levels.

Clearly further information is required on the interaction between other psychotropic and antiepileptic drugs as it is estimated that some 18% of epileptic patients...
attending neurological clinics are also prescribed these medications. Information from this department (Robertson and Trimble, in press) suggests that neither amitriptyline nor nomifensine provoke significant interactions with phenytoin or carbamazepine, although amitriptyline with its tricyclic structure and potential to provoke seizures is clearly unsuitable for use in a population of patients prone to seizures.

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References

The paper that I wrote with Dr Mary Glen-Bott (J Neurol Neurosurg Psychiatry 1984; 47: 960–4) focussed on what was known about the possible epileptogenic properties of viloxazine up to the date of submission for publication, 8 December 1983. The published evidence up to that date suggested that this antidepressant was not contraindicated in epileptic patients. This statement was not meant to be a specific recommendation to prescribe viloxazine, but purely an objective evaluation of one particular risk, namely convulsive seizures, and an assurance for those who use this drug for treating depressed epileptic patients.

We did not discuss other unwanted effects, although we drew attention to the pharmacokinetic interaction between viloxazine and phenytoin. Little is known about this, as it was only fleetingly mentioned in Professor Alan Richen’s chapter in the first edition of Laidlaw and Richen’s Textbook of Epilepsy (Edinburgh: Churchill Livingstone, 1976: 185–233) and it is not mentioned at all in the latest (second edition) of this book. Dr Michael Trimble in his excellent review of non-monoamine oxidase inhibitor antidepressants and epilepsy made reference to this work (Epilepsia 1978; 19: 251). Dr Trimble is right to draw our attention to the most recent work in this field, the unpublished research of Pisani and his colleagues that suggests that viloxazine interacts with carbamazepine to cause “symptoms of carbamazepine intoxication” and that reports a patient who had elevated plasma phenobarbitone levels while being treated with viloxazine. It is difficult for me to comment on these findings as I have not seen the pre-publication manuscript, but I look forward to hearing what symptoms of intoxication occurred (they were presumably Type A reactions) and assessing the evidence leading to the conclusions reached. If it has been demonstrated conclusively that viloxazine increases plasma anticonvulsant levels to a dangerous degree, physicians using the combination should be alert to the possibility of intoxication and should carefully monitor plasma drug concentrations. The interaction should be added to the balance between the chance of benefit and risk of unwanted effects, and should be taken into account when choosing an antidepressant to treat a depressed epileptic patient.

Finally, I agree with Dr Trimble that there is need for much more research into the pharmacokinetic interactions between antidepressants and anticonvulsants in general.

Brain Tumors in the Young

SIR: I wish to comment on the book review by RD Hayward of Brain Tumors in the Young, edited by Luis V Amador. Mr. Hayward has used much of the assigned space to espouse a personal philosophy vis-à-vis subspecialisation in neurosurgery in the United Kingdom, rather than review the volume.

As a full-time pediatric neurosurgeon I feel it is important that there be some response to what I believe is a misguided view. The suggestion that in the United States “where neurosurgeons can lay thick upon the ground—it is perhaps inevitable that pediatric neurosurgery diverge as a separate subspecialty” is unacceptable. No informed neurosurgeon whether specialising in pediatrics or any other facet of neurosurgery would suggest that problems that affect the young are identical to those of the older population. Hydrocephalus, dysraphism, craniofacial anomalies, spinal cord tumours, and even brain tumours are very different in infancy and adolescence in incidence and expression from similar problems that afflict the adult population. Surgical techniques must be directed towards the preservation of the immature growing brain as well as the primary problem and because of these dual considerations are far different from techniques utilised for neurosurgical problems in the adult population.

It is incredible to me that Mr. Hayward suggests that “the head of even a small child is not so different in size from that of an adult, and it cannot be said that the techniques of surgery for the treatment of medulloblastoma and craniopharyngioma are so different either”. This comment not only suggests a complete lack of understanding of the brain of an infant and child (it has nothing to do with size!) but also of these entities and is a testimony to the necessity of training pediatric neurosurgeons to have more insight into pediatric neurosurgical techniques.

Mr Hayward also suggests “in this country, for example, there seem to be enough aneurysms and meningiomas, and pituitary tumours to go around so that no pediatric neurosurgeon can often detach himself from the everyday management of headache and spinal trauma, peripheral nerve wounds, spina bifida, Apert’s etc., not to mention regular presence within the local Pediatric Clinic”. I perceive this statement to be an inaccurate misunderstanding of what the busy, excellent, good neurosurgery really is. I suggest that Mr Hayward is encouraging “general practitioners” in neurosurgery as a whole, and this is clearly out of step with contemporary practice in much of the remainder of the world. There can be little question that surgeons who operate on aneurysms of acoustic neuromas in large numbers have better results than those who do it episodically. The same principle applies to many other surgical diseases of the nervous system.

Mr Hayward’s opinion reflects, I fear, a philosophy that is prevalent in medicine and surgery in the United Kingdom. One can only feel saddened that a country that has produced many pioneers in so many specialties is now unable to evolve with contemporary medicine, and seems to be hermetically sealed in terms of interrelating with what is occurring in much of the world. It would be wise for individuals to explore the value of subspecialisation in terms of what it means to patients, and not to neurosurgeons, before expressing