

a fact that the pubertal spurt may improve not only auxology but also the underlying jejunal pathology. Therefore it is very difficult to analyse auxology of children in such a period. The number of the investigated patients is so impressive that it would be possible to analyse separately those patients who had adhered to a gluten free diet and those who had not complied with this regime.

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## Leukoencephalopathy after prophylactic radiation for leukaemia in ataxia telangiectasia

Sir,

In their short report, Eyre and her colleagues remind readers of the possible harmful effects of therapeutic doses of radiation treatment and tumour chemotherapy in patients with ataxia telangiectasia.<sup>1</sup> Although the radiological appearances in their patients seem consistent with a diagnosis of treatment induced encephalopathy, is it certain that these findings were not those of ataxia telangiectasia itself? What are the findings on computed tomography in children over 5 years with 'uncomplicated' ataxia telangiectasia.

Assuming that this objection can be countered, I wish to challenge the contention, at the end of the report, that '... in children with acute lymphoblastic leukaemia prophylactic cranial irradiation and intrathecal methotrexate should be either withheld or given in reduced dosages'. This recommendation, as far as radiation treatment is concerned, is correct but for methotrexate is misleading and potentially misleading, for the following reasons: Eyre *et al* claim that 'histological examination showed features diagnostic of a *chemoradiation induced* leukoencephalopathy' (my italics); however, so far as I am aware, there is no evidence in the literature that radiation treatment induced and radiation treatment/chemotherapy induced damage in ataxia telangiectasia are histologically distinguishable. Radiation treatment is an acknowledged cause of cellular damage in ataxia telangiectasia, both 'in vitro' and 'in vivo',<sup>2</sup> whereas only a few drugs in clinical use—for example, bleomycin<sup>3</sup>—have been implicated. 'In

vitro' data for other drugs is not readily available but children with ataxia telangiectasia have been reported to tolerate systemic methotrexate/6-mercaptopurine treatment in normal doses.<sup>4</sup> It would be interesting, in the Newcastle case, to know the temporal distribution of the reported 'gaps and reductions' in methotrexate/6-mercaptopurine treatment. If most occurred during the first year of treatment, rather than the second, it may be that lingering radiation treatment induced DNA damage to bone marrow in the craniocervical area, rather than chemotherapy, was blameworthy. A possible increase of vinca-alkaloid induced neurotoxicity has been noted in one report, but is not mentioned in others.<sup>4</sup> This report, which includes a literature review, also contains the specific statement 'No adverse effects from monthly intra-thecal methotrexate were noted in our patients'.

Although ataxia telangiectasia is itself very rare it is relatively more common in the selected group of children who develop acute lymphoblastic leukaemia or malignant lymphoma. While it is clear that radiation treatment must be given in reduced dosage—if at all—to patients with ataxia telangiectasia,<sup>2</sup> and though vincristine is still 'sub judice' it would be unfortunate if intrathecal or systemic methotrexate (or systemic 6-mercaptopurine, asparaginase, or anthracycline) doses were automatically scaled down or omitted. For children with ataxia telangiectasia and acute lymphoblastic leukaemia or lymphoma, the likely outcome would be an increased relapse rate. In many countries children's cancer treatment is now coordinated by national children's cancer study groups. Specific treatment recommendations for children with ataxia telangiectasia and malignancy are needed and could be publicised by these groups (in this country, the UKCCSG).

Incidentally, the terms 'central nervous system prophylaxis' and 'maintenance treatment', as used in the article, are inaccurate and archaic and should be abandoned.<sup>5</sup> 'Central nervous system-directed treatment' and 'continuing treatment' are preferred alternatives.

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Drs Eyre, Gardner-Medwin, and Summerfield comment: Dr Pritchard's points are important ones and we very much agree with his main premise that no form of chemotherapy

that might be life saving should be discarded without sufficient evidence of its neurotoxicity in children with ataxia telangiectasia. We would like, however, to make the following comments in reply.

First, the appearances found on the computed tomogram in our patient are not seen in uncomplicated ataxia telangiectasia and resemble more closely those seen in methotrexate induced encephalopathy<sup>1</sup> rather than in radiation encephalopathy.

Second, the neuropathological changes found in the brain biopsy were 'a variable degree of demyelination accompanied by a florid astrocytic reaction and spongiform change. Small fragments show total necrosis in the absence of a cellular reaction and there is considerable fibrin deposition accompanied by haemorrhage suggesting a subacute vasculopathy of some months standing'. The vasculopathy might well be a feature of radiation encephalopathy but the overall findings are more consistent with those found in methotrexate induced encephalopathy.<sup>2</sup>

As we said in our paper we also regarded the experience of Toledano and Lange<sup>3</sup> as evidence that in ataxia telangiectasia intrathecal methotrexate treatment without cranial irradiation could be followed by neurological deterioration (case 5 in their review). The case report by Abadir and Hakami also suggests that there may be increased sensitivity to methotrexate in ataxia telangiectasia,<sup>4</sup> and in fact Dr Pritchard and his colleagues acknowledged in the discussion following their reported case that there was evidence in the literature of an increased neurotoxicity from intrathecal methotrexate in ataxia telangiectasia.<sup>5</sup>

Dr Pritchard requests further details about the gaps in chemotherapy. In the first year treatment was withheld for 14 weeks and in the second for five weeks. The doses of chemotherapy, however, were decreased in the second year to allow more continuous treatment and thus in the first year the total dose of mercaptopurine was 8680 mg and of methotrexate was 365 mg and in the second year the total doses were 8540 mg and 395 mg respectively. It is unlikely that radiation induced damage to the negligible amount of bone marrow in the craniocervical area was the cause of our patient's intolerance to chemotherapy.

It is clearly very important that any available experience with chemotherapy in children with ataxia telangiectasia should be carefully recorded in the literature as soon as possible. I am sure we all agree that specific recommendations for the treatment of children with ataxia telangiectasia and a malignancy are needed urgently. These perhaps would be best devised and publicised by the UKCCSG. Finally we would like to reiterate our main point that preexisting motor handicap, even if it is mild and apparently non-progressive, in a child with a malignancy should ring alarm bells about possible ataxia telangiectasia.

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## Outcome after antenatal diagnosis of upper urinary tract dilatation by ultrasonography

Sir,

We read with interest the paper by Gunn *et al.*<sup>1</sup> Although they reported a higher incidence of antenatally detected urological abnormalities than in most other published series, their experience in New Zealand is very similar to ours in a district general hospital serving a stable, well defined population in the north of England.

If their results are related to total births, rather than to the number of fetuses examined after 28 weeks' gestation, the incidence of abnormalities was 7/3228, or 2.2/1000 births, 1.6/1000 being pelviureteric junction obstruction.

During the period 1985-7, out of a total of 5762 births, we have found 13 cases of definite urological abnormality, a rate of 2.3/1000. Ten of these (1.7/1000 births) had pelviureteric junction obstruction, two hydronephrosis with megaureter, and one isolated megaureter. All 13 had intravenous urography and were then referred to paediatric surgeons who arranged isotope renography or micturating cystourethrography, or both, when necessary to establish a precise diagnosis.

These results are quite different from those reported recently by Scott and Renwick over the period 1984-6 from the Northern Region Fetal Abnormality Survey,<sup>2</sup> in which we participate. They found only 162 abnormalities in 121 849 births, a rate of 1.3/1000, and of those only 37 (0.3/1000) were 'hydronephrosis' (which we equate with pelviureteric junction obstruction). We have therefore detected many more cases of pelviureteric junction obstruction than this region as a whole, though a similar rate of other urological abnormalities.

Like Gunn *et al* we also found that, where recorded, the maximum dimension of the fetal renal collecting system was 15 mm or greater in all cases that proved to have definite pathology (table).

Table Relation of fetal renal pelvic size to outcome

Outcome	Maximum recorded dimension of fetal renal pelvis			
	<15 mm	15-25 mm	>25 mm	Not recorded
Definite pathology	0	5	9	1
Minor variation				
from normal	4	12	1	3
Normal	7	7	2	4

In some cases each kidney appears separately, therefore the total number is slightly higher than the number of cases.