irrespective of whether these had been classified as symptomatic or cryptogenic. This study gives important information about febrile convulsions in very young children. Eighty three children who had febrile convulsions had had no other abnormality before their onset, and of these, 11 were mentally retarded and 19 had developed epilepsy at follow up, the prognosis being much worse for those babies whose convulsions began before the age of 6 months.

These figures are much worse than those reported in the general population of children with febrile convulsions. They suggest that when such fits occur in infancy the prognosis should be guarded. On a happier note, a form of seizure clinically indistinguishable from infantile spasms but with a normal electroencephalogram and a good prognosis has been described.¹²

Fits in young babies are, therefore, a symptom with very serious implications. A cause should always be sought, and at this age biochemical disorders such as hypocalcaemia, hypoglycaemia, and disorders of amino acid or organic acid metabolism should be considered. Computed tomography is often justified. Pyridoxine dependency must not be forgotten since it is treatable, though rare,¹³ and the possibility of non-accidental injury must be kept in mind—that possibility becoming almost a certainty when retinal haemorrhages are seen.

The part played by immunisation against pertussis in causing infantile seizures is the subject of continuing debate.¹⁴ Chevrie and Aicardi included in their series eight children who had had fits within 36 hours of immunisation.³ In the national childhood encephalopathy study 3.5% of children with encephalopathy and 1.7% of controls had had pertussis immunisation within seven days.¹⁵ The risk of an encephalopathic illness after pertussis immunisation was calculated to be about one in 110 000 injections, and of permanent sequels one in 310 000 infections.

When no cause of the seizures can be found, when the seizures are not infantile spasms, when status epilepticus has not occurred, and when the child is neurologically and developmentally normal after the first fit, then the prognosis is better.

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Cancer, chemotherapy, and fertility

Many young people treated for leukaemia, lymphoma, testicular teratoma, and choriocarcinoma may now expect to be long term survivors. They may, however, become sterile as a result of being cured. Gonadal destruction by cytotoxic agents was first described by Spitz in 1948, who found absent spermatogenesis at necropsy in 27 of 30 men treated with nitrogen mustard.¹ The gonadal effects of cytotoxic chemotherapy are sterility, but usually normal potency, in men and an early menopause, dyspareunia, reduced libido, and premature osteoporosis in women. These side effects are related to the chemotherapeutic agents used, the total dosage and duration of administration, and age and sex.²⁻⁸

The increased survival of patients with advanced Hodgkin's disease is due to treatment with "MOPP" (mustine, vincristine, prednisone, and procarbazine) and its variants.⁹ Two cycles of treatment cause profound oligospermia in all men and this rarely recovers.¹⁰ Follow up of 41 men for up to 12 years showed spermatogenesis in just five, all of whom had been aged under 30 when treated.⁶ Although puberty appears to progress normally in patients treated in boyhood, they usually have azospermia.¹¹ Two studies in women reported contrasting incidences of amenorrhoea (five out of 34¹² and 20 out of 41 patients¹³), but there were differences in the median age and observation period of the two groups. The very small number of girls with Hodgkin's disease treated prepubertally who have been studied were normally fertile.¹¹ An alternative regimen of chemotherapy sometimes used for Hodgkin's disease has been reported to cause less gonadal toxicity: ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) caused azospermia in only six of 17 men, and all 23 women menstruated normally.¹⁴

Treatment of "low grade" non-Hodgkin's lymphoma may have no effect on fertility. Azospermia occurred in all eight men who received over 400 mg in total dosage of chlorambucil.³ The effect may be reversible, however: recovery occurred in five of eight men as early as three months after completing treatment.¹⁵ Three of four men treated with a combination of cyclophosphamide, vincristine, and prednisone subsequently had normal spermatogenesis.¹⁶ Normal spermatogenesis has been reported anecdotally in men treated for "high grade" lymphoma,¹⁷ but no detailed descriptions have appeared of the fertility of women.

The gonadal effects of the treatment of leukaemia reflect both the choice of drugs and the length of time these are given. In one study only one of four men were fertile¹⁸; in another all six men treated with a different regimen for acute lymphatic leukaemia retained fertility.¹⁹ The latter group were treated with intermittent rather than continuous dosages of alkylating agents. Similarly, different results were seen in two studies of boys; in the first, three of 32 prepubertal and five of 12 pubertal boys had abnormal responses to gonadotrophin releasing hormone and all had reduced indices of tubular fertility,²⁰ while in the second all six boys who did not receive cyclophosphamide remained fertile.²¹ Sexual development was impaired in only one of 17 prepubertal girls treated for acute lymphatic leukaemia but it was abnormal in six of 18 pubertal patients, which suggests a relative resistance of the prepubertal ovary to the effects of cytotoxic chemotherapy.²² Men treated with short term chemotherapy for acute myeloid leukaemia have normal spermatogenesis.¹⁸

Patients treated with the Einhorn regimen for disseminated testicular teratoma are likely to be fertile after treatment. Twenty of 24 men had recovery of spermatogenesis 18 months from completing treatment.²³ Fertility is normal in women treated for gestational trophoblastic tumours. In a series of 457 women treated at one centre only seven of 217 wishing to conceive failed to become pregnant.²⁴ Gonadal failure occurs in the treatment of other cancers, but is poorly documented except for breast cancer.^{25,28}

If patients are fertile after treatment no increase is seen in fetal chromosomal damage, fetal abnormality, or the abortion rate.²⁹ For example, the incidences of abortion and fetal abnormality were normal in 368 pregnancies in 217 women²⁴ and in 88 pregnancies in 50 women treated for gestational trophoblastic neoplasms,³⁰ and for 93 conceptions in 29 women and the spouses of 19 men treated for Hodgkin's disease.³¹ Nor were there any abnormal findings in 286 pregnancies in 146 patients (72 of whom had had cytotoxic chemotherapy) treated for a variety of cancers,³² and for 107 pregnancies in 17 men and 29 women who had been treated for cancer in childhood.³³

Might gonadal damage be prevented by storing the germ cells before treatment? Unfortunately not, because fertility is abnormal at presentation. Only 69 of 257 men with either germ cell tumours or Hodgkin's disease had normal sperm counts before treatment.³⁴ Furthermore, more subtle defects may also be present, such that a much greater proportion of patients are functionally sterile; seven of nine men with lymphoma who had normal sperm counts before cryopreservation of their semen had motilities after thawing that were so low that they were considered infertile.³⁵ Comparable changes occur in women; 72 of 87 women with breast cancer had anovulatory menstrual cycles at the time of operation.³⁶ These findings imply that pretreatment storage of germ cells would have only a limited potential.

The possibilities for circumventing infertility may include the more widespread use of non-sterilising treatment programmes, said to be as effective as conventional therapies. For example, fewer treatment cycles may be effective in maintaining remission, but not cause infertility, as in lymphoma.³⁷ Alternatively, adjuvant treatments may protect the gonad. The hypothesis that the resting gonad is less liable to damage by chemotherapeutic agents was investigated in mice which were "protected" by a long acting gonadotrophin releasing hormone analogue.³⁸ This study has been criticised, however, and such compounds were found to be ineffective in dogs.³⁹ Similarly, in men treated at St Bartholomew's and the Christie hospitals there has been no protective effect (Waxman *et al*, submitted for publication).

Physicians should be aware of the possibility of gonadal failure in patients treated for malignancy whether or not cure is expected. Early hormonal replacement therapy for women, except in the sex hormone dependent malignancies, will provide symptomatic relief, easing menopausal symptoms for patients in already sufficiently trying circumstances. In men the relative resistance of Leydig cells makes gonadal failure less likely, but primary erectile impotence may require treatment with androgens.

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