

The histological sections from 108 cases of squamous-cell carcinoma of the cervix treated by surgery were therefore studied. (We are indebted to Dr. A. C. Thackray and Dr. A. D. Thomson, of the Bland-Sutton Institute of Pathology, for the opportunity to study these sections.) Ten cases were excluded because of poor preservation of the nuclei; the ploidy of the remainder was assessed, as before, on the basis of nuclear size. The 10-year cure-rate indicates a significantly better prognosis for the tetraploid class ( $P=0.016$ ) (Table II).

TABLE II

	Alive (No Evidence of Recurrence)	Died
Diploid class	13	31
Tetraploid	25	23

Six patients are excluded from Table II who, though alive and well when last seen, had been followed up for less than 10 years: one diploid and three tetraploid for from 5 to 10 years, and two tetraploid for from 2½ to 5 years. The incidence of glandular metastasis on microscopic examination was significantly higher in the diploid class, and it was noteworthy that of 10 patients with glandular metastasis in the tetraploid class five were nevertheless alive and well after 10 years (as compared with only 1 out of 14 in the diploid class).

It appears, therefore, that the relationship between ploidy and prognosis can be explained in terms of the biological attributes, other than radiosensitivity, of the tumour; tumours in the diploid class are more likely to have spread beyond the limits indicated by the clinical assessment of the disease.

In the course of the present study a correlation has also been found between ploidy and degree of differentiation. When the sections were classified into three grades, following Martzloff (1923), it was found that, whereas most of the tumours in the undifferentiated (spindle-cell) grade were diploid, tetraploid tumours predominated in the other two grades. It is of interest that the relation between ploidy and prognosis appears to be independent of that between ploidy and histological grade. Thus of 182 tumours in the intermediate (transitional-cell) grade, only 17 out of 61 in the diploid group, as compared with 57 out of 121 in the tetraploid group, remained well ( $P=0.012$ ).

Wentz and Reagan (1959), classifying cervical carcinomata into a "small-cell malignant tumour, a large-cell non-keratinizing cancer, and a keratinizing cancer," found a better prognosis for the large-cell and the keratinizing groups than for the small-cell group (the majority of their cases received radiotherapy). Although their classification differs in detail from the present one, their follow-up results probably reflect the same biological principles that underlie the present results.

As mentioned earlier, variation in nuclear size was sometimes seen in the histological sections, and it appears that some tumours, particularly those with a high incidence of endomitosis, have both diploid and tetraploid cells in a more or less intimate mixture. On the other hand, most tumours showed consistency of ploidy even when sections taken from different regions were examined. Perhaps a fair comment on the present findings would be that the influence of ploidy on prognosis may well be more pronounced than appears from the above results, but that the overall picture is modified by variation of ploidy in some tumours.

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## Meclozine ("Ancoloxin") and Foetal Abnormalities

### Preliminary Report by the Epidemic Observation Unit of the College of General Practitioners

In July, 1962, the College set up a Register of Unexpected Toxicity to collect reports from its own members and from others (*Brit. med. J.*, August 11, p. 408) about any association between unexpected toxicity or side-effects in patients (or their offspring) and the previous consumption of drugs, whether new or well known.

Among others so far received, 29 reports have related to mothers who took anti-emetic drugs for nausea or vomiting in pregnancy and who subsequently gave birth to a live deformed baby or suffered the intrauterine death of a foetus. Of these 29 reports, 10 relate to "ancoloxin" (B.D.H.: meclozine hydrochloride and pyridoxine hydrochloride). About pyridoxine, apart from its combination with meclozine, we have registered three other reports. An urgent search was begun on October 16 by a team of nineteen doctors in the College under Dr. P. A. Walford through their records of 784 pregnancies, fully documented as regards drugs, illness, immunizations, and outcome. Most of the patients were attended since September 30, 1961; among these there were 124 mothers who had been given drugs for treatment of nausea or vomiting during the first twelve weeks of pregnancy. Of these, three had malformed babies, and each of these mothers had taken ancoloxin.

The congenital abnormalities registered in our ten reports about ancoloxin are as follows: (1) meningocele; (2) meningocele, hydrocephalus, and bilateral talipes; (3) meningocele, flaccid legs, and patulous anus; (4) spina bifida, microcephaly, and hydrocele; (5) hypoplasia of lungs, kidney, and gall-bladder; (6) imperforate anus; (7) rudimentary thumb; (8) vascular naevus on neck; (9) bilateral talipes; (10) pyloric stenosis.

In view of this mounting evidence against the safety of ancoloxin in pregnancy, information as it was received by the College was passed to the medical adviser of British Drug Houses Limited from time to time, the first six reports being sent on October 22, 1962. It is now felt that the College has a duty to publish the information which has reached it about ancoloxin, in the hope that further investigations can be carried out by others to determine what effect, if any, meclozine and pyridoxine, separately and together, may have upon foetal development. In the meantime the College wishes to draw the attention of all doctors to the information here presented.

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