References

- Costa, G., Hreshchyshyn, M. M., and Holland, J. F. (1962). *Cancer Chemotherapy Reports*, 24, 39.
- Council on Drugs (1965). *Journal of the American Medical Association*, 191, 751.
- Fine, R. N., Clarke, R. R., and Shore, N. A. (1966). *American Journal of Diseases of Children*, 112, 256.
- Finkel, H. E. (1967). *New York State Journal of Medicine*, 67, 2474.
- Grobe, H., and Palm, D. (1972). *Monatsschrift für Kinderheilkunde*, 120, 23.
- Haden, H. T., and Knox, G. W. (1965). *American Journal of the Medical Sciences*, 249, 381.
- Johnson, F. L., Bernstein, I. D., Hartmann, J. R., and Chard, R. L. J. (1973). *Pediatrics*, 82, 699.
- Karon, M. R., Freireich, E. J., and Frei, E. (1962). *Pediatrics*, 30, 791.
- Kleinknecht, D. et al. (1967). *Nouvelle Revue Française d'Hématologie*, 7, 132.
- Loo, H., and Zittoun, R. (1969). *Gazette Médicale Française*, 76, 2693.
- Slater, L. M., Wainer, R. A., and Serpick, A. A. (1969). *Cancer*, 23, 122.
- Whitelaw, D. M., Cowan, D. H., Cassidy, F. R., and Patterson, T. A. (1963). *Cancer Chemotherapy Reports*, 30, 13.

MEDICAL MEMORANDA

Candida albicans Septicaemia during First Half of Pregnancy Successfully Treated with 5-Fluorocytosine

J. SCHÖNEBECK, E. SEGERBRAND

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Cases of intrauterine candida infection during pregnancy are probably very grave and not too rare. They are likely to result in a dead fetus and a spontaneous abortion (Albarracin *et al.*, 1967; Aterman, 1968; Lopez and Aterman, 1968; Ho and Aterman, 1970). In these cases the infection is generally believed to ascend from the vagina. Cases of yeast fungus septicaemia during pregnancy are probably extremely rare. However, they present great therapeutic problems, as the antimycotic drugs available—above all amphotericin B—are so toxic that their use involves a great risk for the patient and probably an even greater risk for the fetus.

We recently treated a case of *Candida albicans* septicaemia during pregnancy successfully with 5-fluorocytosine (5-FC).

Case Report

A 22-year-old woman suffered from hyperemesis gravidarum during her first pregnancy in 1970 which ended in spontaneous abortion. In 1971 she was again pregnant, having had her last menstruation on 3 November 1971. At the end of December she suffered from a pronounced hyperemesis gravidarum, which necessitated admittance to hospital. Her symptoms grew worse and intravenous nutrition had to be given. A central venous catheter was placed in the superior vena cava and remained there until 22 February 1972. At the end of January 1972 she got septic fever. Ampicillin was given intravenously, and the temperature was temporarily reduced. On 9 February, however, she got chills and rising septic fever. Cloxacillin treatment was then instituted. Blood culture at that time showed a pure culture of *C. albicans*, and oral nystatin treatment, 1,000,000 I.U. three times daily, was started. The fever was slightly reduced, but on 16 February the patient again got chills and her general condition was strongly affected. Again blood culture showed a pure culture of *C. albicans*. The nystatin administration was stopped, and on 16 February 600 mg of 5-FC was given as an intravenous infusion. On 17 February this treatment was substituted by oral administration of 5-FC, 2 g four times daily. Next day she was free from fever. Her general condition improved rapidly,

and she was able to take food per os. The central venous catheter was removed on 22 February. Culture from the tip of the catheter showed growth of *C. albicans*. The patient recovered completely and was discharged on 17 March. She had received a total dose of 52.6 g 5-FC.

Even before the institution of 5-FC therapy the patient's SGPT values were increased. After stopping the treatment they returned to normal. The complement fixation test for *Candida* was positive. On 21 February the serum concentration of 5-FC was 25 µg/ml.

Subsequently the patient's pregnancy advanced quite normally, and on 25 July 1972 she gave birth to a normally developed girl (birth weight 2,940 g, length 48 cm). The child's progress was followed in the usual manner during the first seven months after delivery and was completely normal.

Comment

There is no doubt that the central venous catheter was the cause of the patient's candida septicaemia. It was removed during the course of treatment, and on culture from the tip of the catheter there was growth of *C. albicans* in spite of adequate serum concentration of 5-FC (25 µg/ml). The reason for this is that the antimycotic drug does not reach adequate concentration on the surface of a foreign body. Thus, in intravenously nourished patients who develop yeast fungus septicaemia, the first step to be taken should be to remove or exchange the central venous catheter.

Yeast fungus septicaemia during early pregnancy is probably not a common condition. In reviewing the literature we have found only one similar case. This also occurred in connexion with a severe hyperemesis which necessitated intravenous nutrition. To save the patient first an abortion was induced and then amphotericin B treatment given. In this case the fungus was *Torulopsis glabrata* (Hahn *et al.*, 1968).

In these cases the problem of appropriate treatment is a very difficult one. Until now there has been nothing but amphotericin B treatment to be given. This preparation is effective against the fungus, but it is so toxic that many physicians hesitate to give it to children (Holt and Newman, 1972). If it has to be given to a pregnant woman it therefore seems reasonable to induce an abortion because of the toxicity of the drug. This should be done when the patient's fungus septicaemia has been cured and her general condition has improved.

5-FC has proved to be an excellent antimycotic drug (Scholer, 1970; Schönebeck, 1971, 1972) with few and as a rule not serious side effects. However, Bennett (1971) and R. Y. Cartwright (personal communication, 1972) have reported bone marrow and liver toxicity. The teratogenic effects of 5-FC have been studied by Chaube and Murphy (1969). They found that intraperitoneal administration of 500-4,000 mg/kg body weight to rats on the 11th or 12th day of gestation resulted in fetal deformities—mostly cleft palates, micrognathia, and short, kinky tails. If the drug was administered on the 9th or 10th day there were no deformities. The lowest teratogenic dose was 700 mg/kg body weight. The therapeutic dose of 5-FC in normal kidney function is about 50 mg/kg body weight every

Departments of Urology and of Obstetrics and Gynaecology, University of Umeå, Umeå, Sweden

J. SCHÖNEBECK, M.D., Assistant Surgeon
E. SEGERBRAND, M.D., Assistant Surgeon

6th hour (Schönebeck *et al.*, 1973)—that is, much less than the lowest dose with teratogenic effects in rats. Of course it cannot be excluded that the drug might have a teratogenic effect in man at a lower dose.

Our patient was informed of these facts. Yet she was strongly determined to carry her pregnancy through, and 5-FC therapy was definitely indicated because of her septicaemia. It should be emphasized that the pregnancy had advanced past the period of gestation most dangerous from the teratogenic point of view.

As her SGPT values were raised even before the institution of 5-FC treatment it is not likely that 5-FC should have caused the rise in transaminase. It was probably a result of liver toxicity from the candida septicaemia.

Like most other drugs 5-FC should not be given to women during early pregnancy. If a patient develops a yeast fungus septicaemia in early pregnancy and if there is strong indication for keeping the pregnancy going, we find 5-FC to be the safest preparation for the time being.

References

- Albarracin, N. S., Patterson, W. S., and Haust, M. D. (1967). *Obstetrics and Gynecology*, 30, 838.
 Aterman, K. (1968). *American Journal of Clinical Pathology*, 49, 798.
 Bennett, J. (1971). *Antimicrobial Agents and Chemotherapy*, 1970, 10, 28.
 Cartwright, R. Y. (1972). Personal communication.
 Chaube, S., and Murphy, M. (1969). *Cancer Research*, 29, 554.
 Hahn, H., Condie, F., and Bulger, R. J. (1968). *Journal of the American Medical Association*, 203, 115.
 Ho, C. H., and Aterman, K. (1970). *American Journal of Obstetrics and Gynecology*, 106, 705.
 Holt, R. J., and Newman, R. L. (1972). *Developmental Medicine and Child Neurology*, 14, Suppl., p. 27.
 Lopez, E., and Aterman, K. (1968). *American Journal of Diseases of Children*, 115, 663.
 Normark, S., and Schönebeck, J. (1972). *Antimicrobial Agents and Chemotherapy*, 2, 114.
 Scholer, H. (1970). *Mykosen*, 13, 179.
 Schönebeck, J. (1971). *Proceedings of the Fifth Congress of the International Society for Human and Animal Mycology*, p. 292.
 Schönebeck, J. (1972). *Scandinavian Journal of Urology and Nephrology*, 6, Suppl. No. 11.
 Schönebeck, J., and Ansehn, S. *Sabouraudia*. In press.
 Schönebeck, J., Polak, A., Fernex, M., and Scholer, H. *Chemotherapy*. In press.

Expanding Skull Fracture of Childhood

D. P. ADDY

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Expanding skull fractures in children have been described for many years, but mostly in specialist neurological or radiological journals or in overseas journals (Lende and Erickson, 1961; Bandi *et al.*, 1969; Gruber, 1969; Goldstein *et al.*, 1970; Adeloje, 1971). The purpose of this report is to bring the condition to the attention of a wider readership.

Case Report

A boy aged 1 year 4 months was admitted to hospital having fallen from a first floor window on to a hard surface. His birth and progress to the time of the accident had been normal. On admission he was deeply unconscious, pale, and sweating and had a large haematoma in the right occipital region of the scalp. An x-ray picture showed a long linear fracture in the right parietal region of the skull (fig. 1). Frequent right-sided convulsions were treated with intravenous phenytoin sodium, and the child gradually regained consciousness over the next three days. He was then found to have a mild left-sided hemiparesis and a left homonymous hemianopia.

He was next admitted to hospital aged 2 years 8 months because of a prolonged left-sided convulsion, having been previously well since the time of the accident. There was now a palpable defect in the right parietal region of the skull and a corresponding defect was seen on an x-ray picture (fig. 2). Repeat x-ray examination 21 months later showed the defect to be unchanged (fig. 3).

After the second admission the child remained free of fits for 19 months on phenytoin sodium, but then developed brief left-sided clonic fits without loss of consciousness which rapidly increased in frequency up to five a day. The addition of phenobarbitone and sulthiame in turn to the anticonvulsant therapy produced no improvement, but the attacks stopped soon after giving acetazolamide, and at the time of writing he has been free of attacks for nine months on phenytoin sodium and acetazolamide.

FIG. 1—X-ray picture of skull at time of first admission.

FIG. 2—X-ray appearance at time of second admission.

Department of Paediatrics, Dudley Road Hospital, Birmingham B18 7QH

D. P. ADDY, M.B., M.R.C.P., Consultant Paediatrician