SUMMARY

A 6 patients (five pregnant women and one not pregnant) already highly sensitized with obstetrics history of erythroblastosis are presented. Demonstrating the use therapeutic of chemical agents (6-Mercaptopurine, Azathioprine, Prednisone, Cyclophosphamide, Cytosine arabinoside) as a means of immunosuppression of anamnestic Rh-immune response. Suppression of this anamnestic response have been beneficial in all cases but one, by this method immunoparalysis. In the case not pregnant, is reported a desensitization down to make the titer of the indirect Coombs test negative, then hope for future pregnancies in these highly sensitized women might be theoretically offered. Methods for producing a state of immunologic tolerance in the Rh problems.

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The effect on Rh$^+$ new borns of immunosuppressive drugs administered to their Rh$^-$ mothers during pregnancy. A pediatrician's viewpoint

by

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In recent years, clinical research on the effects of immunosuppressive drugs administered during the course of pregnancy has been carried out by Onnis and co-workers. The drugs were administered on a continuous basis during the last 20 weeks of gestation to women with unoperable neoplasms, and the newborns of these mothers showed no apparent effects as a result of this treatment ([1]).

Later, using the same substances, Onnis treated pregnant women who had a

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high Coomb's titre along with significantly high foetal levels of bilirubin as revealed by amniocentesis.

The Author has the opportunity to examine a number of newborns from mothers treated with immunosuppressive drugs and has previously written several papers on this subject ([2, 3, 4, 5]).

The present communication reports the wiewpoint of a Pediatrician regarding the outcome of this treatment in 10 neonates with hemolytic disease born from mothers treated with 6-mercaptopurine or ametopterin during the last 10-20 weeks of gestation.

Treatment of these women was decided upon by an obstetrical team after a careful evaluation of the underlyng ethical rational of this problem.

CASE STUDIES AND METHODS

The subjects studied in this report consisted of a group of 10 full-term newborns suffering from erythroblastosis foetalis due to Rh immunization.

The anti-D titres were determined in the mothers during the course of pregnancy by means of the indirect Coomb's test, and the maximum titre was between 256-512 in all cases. Total bilirubin and conjugated bilirubin were determined according to Malloy and Evelyn ([6]).

Six infants born to mothers treated with ametopterin (2.5 mg per day) and 4 others from mothers treated with 6-mercaptopurine (100 mg per day) were examined. Care was taken to compare the effects of the immunosuppressive treatment on the bilirubin level of these newborns with respect to a control group of 10 fullterm infants suffering from erythroblastosis foetalis whose mothers did not receive these drugs during pregnancy. The Coomb's titre of this latter group was in the same range as that of the experimental group.

RESULTS

Frequency of exchange transfusions: all subjects underwent one or more such treatments and all survived.

Serum bilirubin concentration: the course of the total bilirubin concentration was similar in the two groups, as were also the red cell and reticulocyte counts and the haemoglobin and hematocrit levels. In contrast, the newborns of mothers treated ith immunosuppressive drugs showed lower levels of conjugated bilirubin.

DISCUSSION

This investigation demonstrated that all the neonates required one or more exchange transfusions, regardless of whether the mothers received immunosuppressive drugs or not. The course of the hemolytic disease was not significantly different in either group, even though a lower level of conjugated bilirubin was observed in theh blood of the treated group (Fig. 1). This can be attributed to an inhibition of bilirugin-UDP-glucuronyl transferase enzyme by the immunosuppressive drugs, substances which are able to pass across the placental barrier. In fact, it is well known that foetal bilirubin-UDP-glucuronyl transferase is activated by the increased level of unconjugated bilirubin found in foetuses suffering from erythroblastosis foetalis ([7]).

The immunosuppressive effect of ametopterin and 6-mercaptopurine on the

foetus was also evidenced by the decreased concentration, or even total absence, of IgA and IgM along with a pronunced decrease in IgG with respect to the controls ([2]). On the other, the aforementioned drugs do not exert any effect, at least in the doses employed, on the maternal and foetal serum complement concentrations ([5]).

Preliminary investigations of the mechanism of cellular immunity, as studied by means of the transformation of peripheral lymphocytes into blast cells when

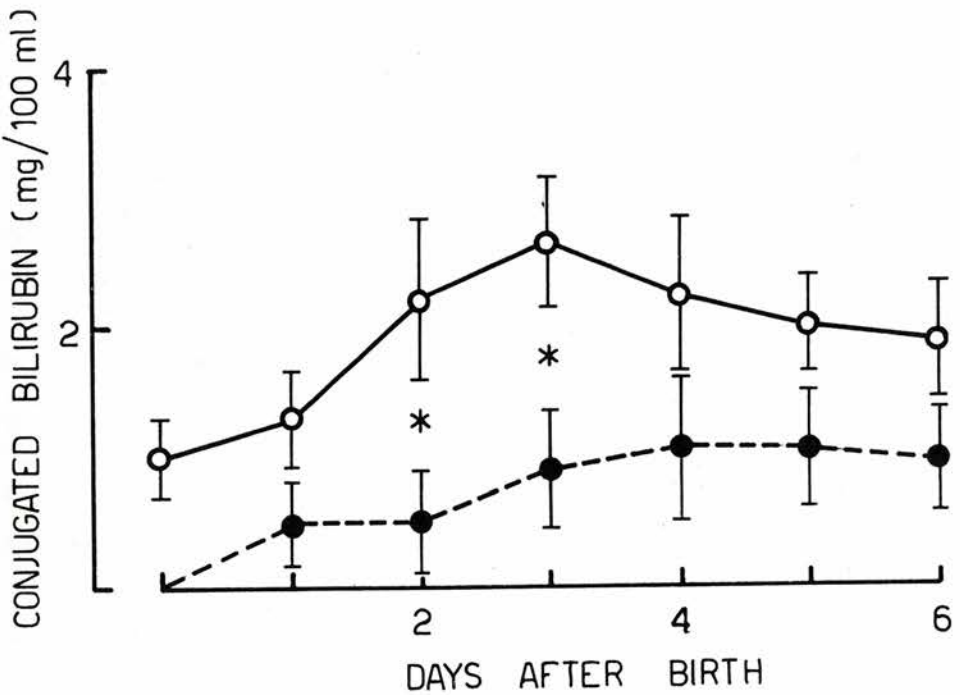

FIG. 1 - Conjugated bilirubin in serum from newborns of mothers treated with immunosuppressive drugs (●) and from newborns of untreated mothers (○) *$p<0.01$.

cultured « in vitro » with phytohemagglutinin, have not demonstrated significant differences in activity between the controls and newborns of mothers treated with immunosuppressive drugs ([8]).

Careful clinical and neurological examination were performed on all the infants in order to evaluate the possible adverse side effects of the immunosuppressive drugs. At birth none of the examined infants showed any pathologcal signs attributable to these drugs. Their weight, as related to gestational age, was similar to that of the control group, demonstrating that these drugs administrated to the mothers during the last 10-20 weeks of gestation, do not interfere with normal intrauterine development. Long term follow-up studies are currently being carried out and the results will be reported in a subsequent communication.

On the basis of the presently reported data, it is not possible to draw any conclusion regarding the ultimate innocuousness of this treatment. Only long

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term controlled studies will permit a precise evaluation of the possible risks inherent in same.

It seems reasonable to conclude, therefore, that this treatment has no favourable influence on the prognosis of infants suffering from erythroblastosis foetalis. At

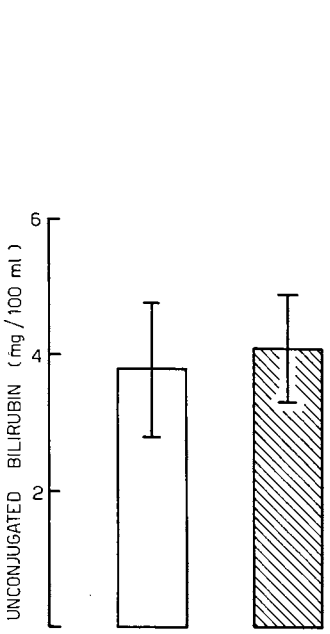

Fig. 2

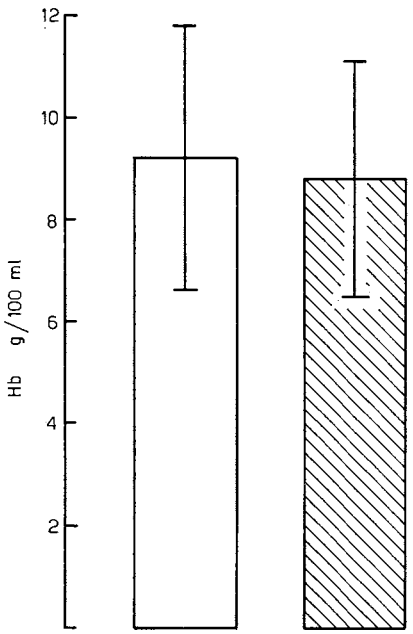

Fig. 3

Fig. 2 - Unconjugated bilirubin at birth in infants born to mothers treated with immunosuppressive drugs (●) and in infants born to untreated mothers (○).

Fig. 3 - Haemoglobin level at birth in infants born to mothers treated with immunosuppressive drugs (●) and in infants born to untreated mothers (○).

present, the only hope for a definite resolution of this problem rests in the ample prophylaxis of the mothers by means of treatment with specific immunoglobulins in order to prevent the occurrence of Rh immunization.

SUMMARY

Were examined six infants born from mothers treated with amethopterin and four others from mothers treated with 6-mercaptopurine. All infants were suffering from erythroblastosis foetalis. It is not possible to draw any conclusion regarding the innocuousness of this treatment.

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Fluorescence of nile blue sulphate in amniotic fluid cytology

by

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INTRODUCTION

Amniotic fluid cells are primarily examined to diagnose rupture of the membranes and to evaluate foetal maturity. Nile blue staining is helpful for both these purpose, although with some disadvantages. Orange-stained cell counts are influenced by clumping of the cells and by consequent difficulty of differentiating large drops of extracellular fat from foetal squamae. Interpretation may also be impeded by stain or crystal deposits, or by the presence of maternal squamae. The increase of lipid cells in the later stages of pregnancy has also been differently reported in the literature.

Earlier work ([3]) showed Nile blue sulphate fluorochroming for cell components and extracellular material stained orange in ordinary light microscopy; these are probably neutral fats. The present paper reports results observed in an investigation designed to show whether this feature of the dye is of assistance in increasing the accuracy of the methods proposed by Kittrich ([2]) and Brosens & Gordon ([1]) for the determination of foetal maturity and membrane rupture respectively.

MATERIALS AND METHODS

Foetal maturity was assessed from amniotic fluid sediments obtained during caesarian section (31 patients with unruptured membranes), by transabdominal amniocentesis in 18 cases of Rhesus incompatibility, and as a result of vaginal amniorrhexis via the amnioscope (38 cases). Contamination with cervical and vaginal material was virtually nil when the last method was amployed. To assesment of maturity were made:

a) by assessing the percent of orange-stained cells presentig counts of 300 cells under the ordinary light microscope;

b) by grading (from 0 to 4) the number of isolated or masses lipid cells and drops of extracellular fat observed in fluorescence microscopy.

The failure to observe non-lipid material, of course, prevents a differential

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