cocious that changes of urinary excretion of total estrogens. Perhaps blood determination will shown changes even more precocious.

This report show a parallelism in decrease between urocytogram and total estrogens excretion in patients with recurrent abortion. The cytohormonal changes of urinary tract cytology are, with these results, more precocious that estrogens alterations and the Autors think that it is as result of all maternal hormonal milieu whose interrelationships can show themselves before of only estrogens determination.

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# Functional platelet activity in pregnancy and the newborn period

by

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We studied platelet activity during normal pregnancy, including the peripheral platelet level, thromboplastin activity, platelet aggregation reactions with collagen, ADP, adrenalin and the adenine nucleotide level. In the newborn the studies also included investigation of the third platelet factor and the TGT (thromboplastin generation test).

Our case material consisted of 30 multipara in all three trimesters of normal pregnancy and 15 infants from these patients; the various functional characteristics of the platelets were examined in the infants at birth, and on the 8th and 20th day after birth.

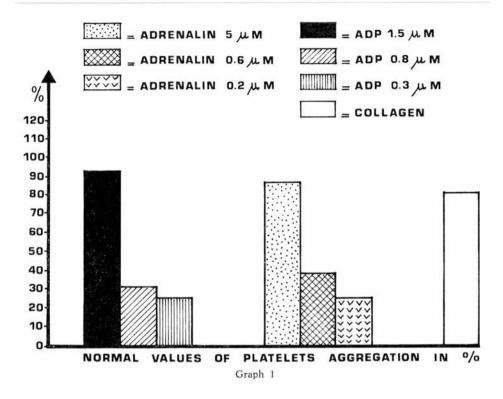
The results obtained with the women in the first trimester were the same as those obtained with the non-pregnant patients of the same age who acted as controls (see graph 1).

The results obtained with the pregnant women in the second trimester showed an increase in the platelet count in the blood; acceleration of the thromboplastin formation curve (in 24 out 30 cases maximum thromboplastic activity at 4 min)

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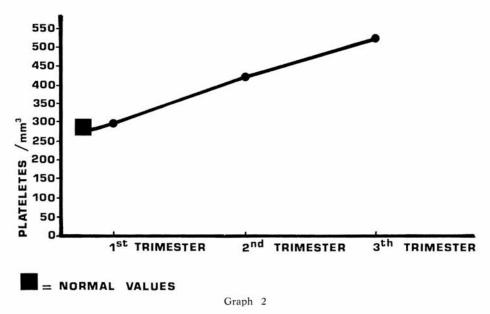
moderate increase in platelet aggregation with ADP and adrenalin at the three concentrations; with collagen the percentage of aggregation was normal in most cases, although a protracted latency period was observed in some cases; an increase in the adenine nucleotides (ATP, ADP, AMP and ATP/ADP ratio), which increased as the pregnancy progressed, was also noted (see graphs 2, 3, 4, 5).

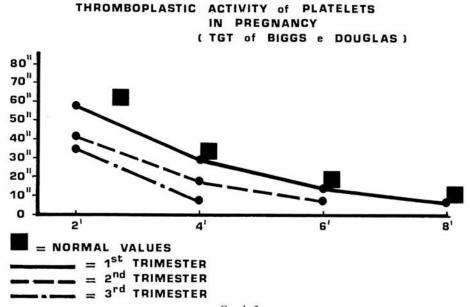
During the third trimester of pregnancy, near the time of birth, a further, consistent increase in the blood platelet count occurred; the endogenous throm-boplastic hyperactivity (exceeding the values obtained during the second trimester) persisted. The platelet reactions showed a further rise in the aggregation curve with the ADP inductors and adrenalin at the three concentrations. In contrast, the collagen inductor revealed a hypo-aggregation disorder, with an increase in the latency period in six cases (see graphs 2, 3, 4, 5).

The findings obtained with the infants can be summarised as follows:

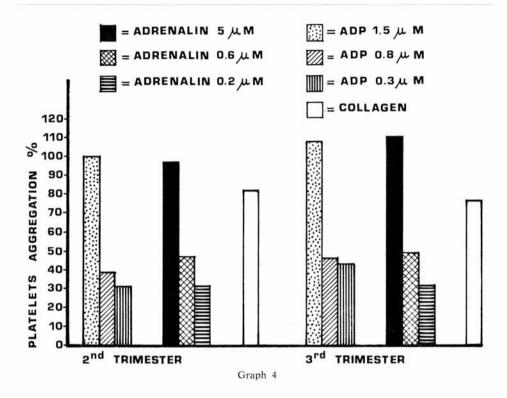
- a) normal blood platelet values at birth, reduction on 8th day after birth (200,000-230,000) and return to above-normal values on the 20th day after birth (350,000 on average).
- b) definite thromboplastic platelet torpor, partly corrected by treatment with PRP (platelet-rich plasma), kaolin, and kaolin with ADP (see graph 6); even at the time of birth the thromboplastin torpor persisted in the PRP; this had become attenuated by the 8th day after birth, and was entirely corrected by treatment with kaolin and kaolin together with ADP. The consumption of prothrombin supports these findings and reveals the persistence of a moderate

## PLATELETS IN NORMAL PREGNANCY





Graph 3



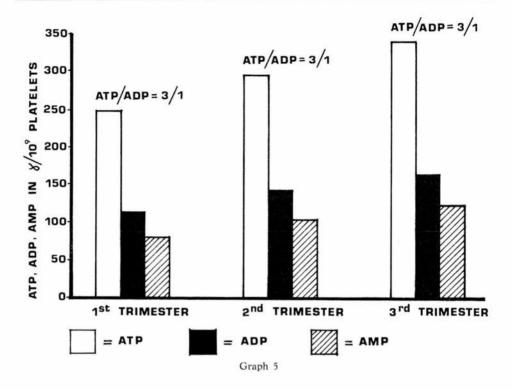
thromboplastic deficit in the PRP, but no longer in the TGT. On the 20th day after birth thromboplastic function appeared to be normal and treatment with kaolin, and with kaolin together with ADP, further inhibited thromboplastic activity, up to thrombophile values.

- c) Although the adenine nucleotides showed a gradual increase up to the 20th day after birth, during this period we also observed an overall deficit and a deficit in the ratios; the ratio reduction was greatest for ATP (see graph 7).
- d) The platelet aggregation percentage in the first 20 days after birth revealed a gradual increase in ADP (8th day) and in adrenalin (20th day); collagen however never attained average values, leading to a hypo-aggregation disorder which extended to the end of the neonatal period (see graph 8).

The functional aspects of platelet activity in normal pregnancy thus showed, in the last two trimesters, a state of hyperactivity in regard to numerical increase, thromboplastic activity and in the platelet reactions to the three inductors; in the light of our present knowledge, this state of hyperactivity can be classified as « a tendency towards a state of thrombophilia ».

It must be streassed that the increase in platelets is attributable to hyperactivity of the maternal thrombopoietic hormone, which also regulates foetal thrombopoiesis.

The functional platelet variations can probably be ascribed to acceleration and release into the circulation of recently formed platelets, in association with special environmental situations, i.e. protein, lipid and hormone variations characteristic of the particular period of pregnancy. Thus, the platelet hyperaggre-



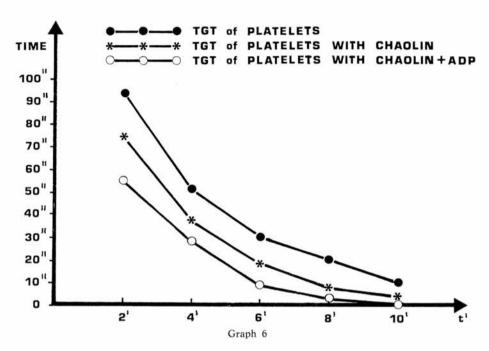
gation may be explained by the increase in plasma globulins and in fibrinogen (these proteins show a marked surface activity in relation to the platelet membrane with consequent aggregation hyperactivity), and also by the increase in very low-density lipoproteins, which are the principal carriers of glycerides (1-6). At present it seems that, in pregnancy, hyperglyceridemia is due to an increase in circulating estrogens; this leads to a state of platelet hyperaggregation dependent on the increase of lipids (triglycerides) in the plasma (always resulting from changes in membrane stimulus), or on an increase in estrogen-dependent intraplatelet lipid synthesis. Recently tests with thromboplastintype endogenous phospholipids have demonstrated their metabolic synthesis routes in the presence of Co-A and ATP, always with changes in membrane stimulus.

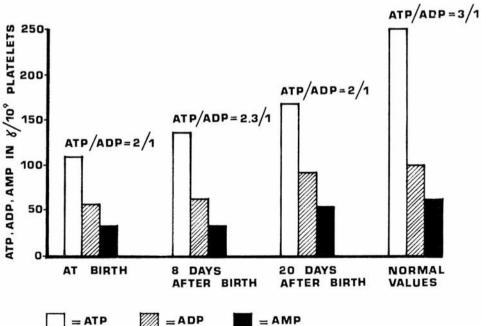
In view of the fact that the newborn responds with a state of platelet hypoaggregation to the three inductors tested by us (ADP, collagen, adrenalin), we find that in regard to the thrombopoietic system the maternal-fetal relationship shows a divergence in physiological condition.

The reduced platelet function in relation to thromboplastin formation, the decrease in prothrombin consumption, the decrease in adenine nucleotide content, the overall lack of aggregation despite the normal peripheral platelet level suggest a metabolic platelet change which affects the endogenous metabolic-enzyme reserve, as well as changes in the platelet membrane.

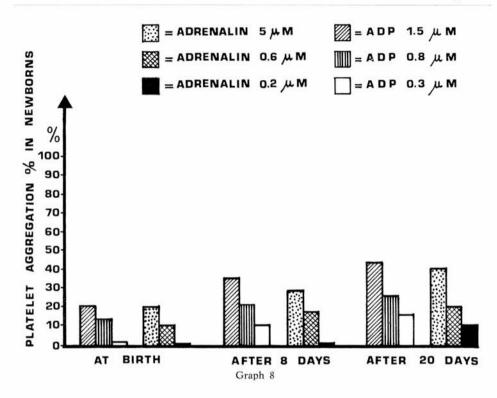
We are thus dealing here with a true « functional platelet meiopragia of the neonatal period », attributable to the state of endouterine anaerobiosis, which

#### NEWBORNS AT BIRTH





Graph 7



reduces the intra-platelet oxidative route and thus results in a decreased production of ATP.

### SUMMARY

The authors report the results of a study on platelet function in the maternalfetal relationship, in normal pregnancy. A clear divergence between the situation of the mother and that of the infant was found in relation to the thrombopoietic system.

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