CONCERNING A NEW PATHOGENETIC HYPOTHESIS OF THE E.P.H. GESTOSIS (Note II)

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SUMMARY

In this second note, the Authors report a new therapeutic protocol, based on the aetiopathogenesis, of the E.P.H. gestosis, which allows an efficient clinical control of this disease, avoiding its evolution to eclampsia.

The gestosis is a disease due to missed materno-foetal adaptation, consequent to the activation of the immunocompetent system of the maternal guest, against the "not self" antigens carried by the trophoblast.

It is also due to missed destruction of the tunica media of the placental bed's arteries and to the thromboplastinic activity of the trophoblastic cells damaged by the immunologic reaction.

In fact this disease represents the clinical and morphologic appearance of a "temporaneous" (preeclamptic gestosis) or "definitive" (eclamptic gestosis) defeat of the fibrinolytic control mechanism against a disseminated intravascular coagulopathy (D.I.C.).

It must be explained that the clinical damage and the degrees of D.I.C. depend not much on the entity of the trophoblastic and parieto-vasal damage, as rather on the dinamic relation between liberation of factors having thromboplastic activity and activity of the fibrinolytic control system.

On the basis of what is just mentioned it is possible to propose a therapeutic protocol based on the aetiopathogenesis, which acting on the various phases of the gestosic process modifies it, avoiding the dramatic evolution to the eclamptic form [1, 2, 5, 6, 10, 11, 12, 13, 14, 15, 18, 20].

The therapy will have as main aims:
— the control of the immunologic reaction [7, 16]
— the control of the thromboplastinic activity [19]
— the control of the utero-placental arteriolar vasospasm [8, 17]
and as secondary aims:
— the detoxication of the maternal organism [3]
— the control of the eventual damages to the foetus [17]
both in mild and severe forms.

With the purpose of a therapeutic attempt on out-patients it will be possible to administer hCG at doses of 1000-5000 IU every second day and cortisone at

doses of 2-4 mg/day or every second day, starting from the 30th week of gestation, preferring Triamcinolone, for it is a drug with poor tubular-retentive capacity.

A haemocytometric examination with an haematocrit and count of thrombocytes and dosage of the FDP (fibrinogen degradation products), together with an electrophoretic protidogram and serial urine examination, will permit a serious management of the disease in the out-patients.

The control of eventual oedemas will be performed using drugs blocking Aldosterone, while the pressure values will be reestablished by the only use of vasodilators: nicotinamide (50-300 mg/day).

In case of severe forms up to the so called pre-eclamptic gestosis, the patient will be hospitalized.

The corticosteroids will be administered up to doses of 8 mg/day according to the various clinical parameters, while the doses of hCG will reach the 10.000 IU/day; an infusional therapy with albumin will also be performed.

The reestablishment of the oncotic pressure and the subsequent haemodilution in controlling the form will be mostly efficient, while the continuous infusion of β-stimulants will be performed to control the eventual uterine spasm.

The therapy reaches its maximum utilization only in case of severe pre-eclamptic and eclamptic gestosis.

After having determined the haematocrit, the protidogram and the FDP, the treatment will include:

a) corticosteroids
b) heparin
c) plasma expanders
d) β-stimulants
e) Mg sulphate

while a catheter introduced in a peripheral vein will allow to measure the C.V.P.

In fact it must be pointed out that any shock induces an increase in the haematocrit, a reduction of albumin and an increase in globulins and fibrinogen.

As a consequence there will be a rise in the haematic viscosity, a slowing of the capillary circulation and a hastening of the sludging's phenomenon. The vasoconstriction will then increase the stasis worsening the ischemia.

It is therefore evident that the administration of substances which can dilute the blood reducing its viscosity, can only facilitate its passage through the narrow vessels and reduce the ischemic damages.

In this case, 1 gr/Eq of hydrocortisone every eight hours, will exert a favourable effect improving the circulatory conditions and stimulating the diuresis.

It must be pointed out that, till nowa days, the real mechanism of action of the corticosteroids is still unknown, even if it is clear that they have a generic protecting effect on the cells affected by ischemia and hypoxia and that they reduce the response of the smooth muscles to catecholamines. An other suspected effect of corticosteroids would be the possible immunomodulation which would lead to a decreased lymphocitary activation against the trophoblastic cells.

The basic factor of the antiaggregating therapy will be heparine, which blocks the D.I.C. and reestablishes the fibrinolytic control.

From 50 to 100 U/Kg of heparine will be administered every six hours in order to maintain the prothrombin test around 20-22% of the normal value, while the administration of epsilonaminocaproic acid will avoid the risk of dangerous thromboembolisms.

The dosage of the FDP will indicate when the fibrinolytic system has reestablished the control of the situation.

An other factor of the therapy will be represented by the use of plasma expanders. Among these we point out the compound formed by gelatine and polysaccharides.

The administration of Rheomacrodex at doses of 4 g/Kg reduces sensibly the haematic viscosity, lowers the haematocrit

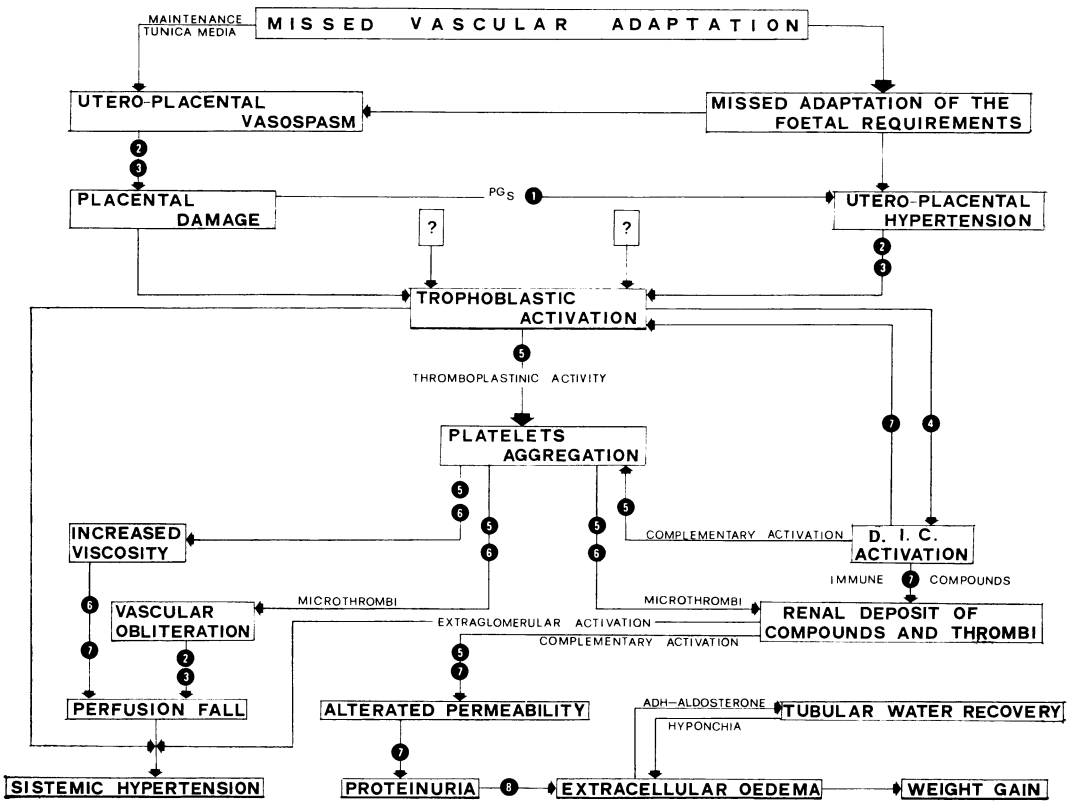

Fig. 1. — Shows the probable pathogenetic mechanism of the E.P.H. gestosis. Numbered the possible therapeutic control: 1) Anti PGs agents; 2) Beta-stimulants; 3) O_2; 4) hCG; 5) Heparin; 6) Plasma Expanders; 7) Corticosteroids; 8) Albumin.

and decreases of 30-35% the peripheral resistances, increasing of about 30% the capillary flow.

The use of β-stimulants in continuous infusion will be essential to control the utero-placental vasospasm.

The use of suppositories at 50% of Mg sulphate, will permit to obtain, even in presence of mild cerebral oedemas, a gradual and prolonged decompression. The administration will be repeated twice a day, and the maximum effect will be obtained after 3-4 days.

Besides the major therapeutic factors, albumin, cardiokynetics and various drugs, necessary on the basis of the indications of each single case, will be used.

Finally, in order to resolve completely the case, it will be necessary to induce the delivery, even using prostaglandins administered transcervically intramurally.

Finally, the therapy of the eclamptic gestosis must be mentioned, which is substantially the same used in severe pre-eclamptic gestosis, adding drugs necessary to control the uncoordinated motion activity.

Thiopentane and curare are the most important ([4]).

The first blocks the external factors which can cause an attack, the second an-

nullates the muscle motility. In this way, the patient with eclamptic attacks will be curarized and artificially ventilated with O_2, at concentrations cardiotopographically active.

It is possible to use urea in a 30% solution in 10% of glucose, in order to reduce the intracranic pressure, reminding that its use will have to be modulated on the basis of the residual renal activity, and that, the use of the latter, in presence of a severe renal damage, must be avoided.

We retain to have treated the most adequate gestosis therapy, on an aetiopathogenetic basis, and we are convinced that, if applicated and modified in function of the new pathophysiologic experience, it can contribute to resolve severe forms of gestosis.

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