Clinical Experimental Obst. & Gynecology
Vol. III, 1-4, 1976 pp. 62-66

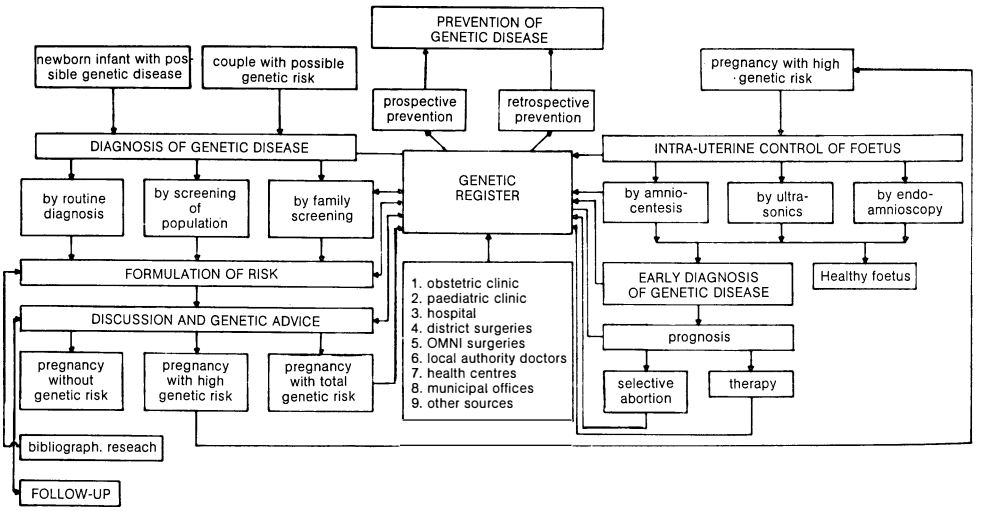

FIG. 3 - Organization scheme for a research unit for the diagnosis and prophylaxis of hereditary and chromosomal diseases.

derived from the central records will enable the risk to be formulated, and genetic advice to be given. At present, pregnancies that carry « no genetic risk » (the risk being no greater than is foreseeable for any pregnancy) leave the circuit which involves the genetic centre; those listed as « total risk » follow a shorter circuit, concerned with the prevention of the birth of an affected child, whose characteristics are supplied to the central registry; and finally, the pregnancies of « high genetic risk » are dealt with by second-stage intervention, involving pre-natal checks by the methods we have already illustrated. The early diagnosis *in utero* of « genetic diseases » will in its turn lead, whenever possible and convenient, to adequate therapy; where this is not possible, the prevention of the birth of a diseased foetus can only be brought about by genetic abortion.

Serum and placenta levels of cholestasis enzymes in pregnancy

by

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Various methods are presently available to diagnose intra and extrahepatic cholestastasis. Chemical analyses used mainly involve bilirubin and cholesterol levels

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Acknowledgements: The authors wish to thank Mr. G. Ricci and Miss N. De Venuto for the skilled technical assistance.

This work was supported by a grant from C.N.R. N. 75.00456.04

and iron/copper ratio in serum. The most sensitive enzymatic tests for indicating the presence of cholestasis are γ-glutamiltranspeptidase (γ-GT) ([1,2,3]), alkaline phosphatase (PHA) ([4,5,6]), leucineaminepeptidase (LAP) ([7,8,9]), and 5'-nucleotidase ([10,11,12]).

The present study has been made of cholestasis enzymes during pregnancy. This seemed important for at least three reasons: 1) because alterations in liver function can be seen during pregnancy without a purely pathological state, 2) because some authors ([13,14,15]) maintain that minimum of intra-hepatic cholestasis is always present in physiological pregnancy, and 3) because testing the activity of these enzymes at different times would make it possible indicate the enhancement period of PHA and LAP ([16,17,18,19]). At the same time, it seemed interesting to compare their behaviour with that of γ-GT, which has not yet been well defined in pregnancy.

Along with these analyses, examination was also made of PHA, LAP and γ-GT content in placenta, in order to study the importance of this organ in the increase of these enzymes in serum during physiological pregnancy.

MATERIALS AND METHODS

Study was made of 56 normally pregnant women: 13 in the first trimester, 6 in the second and 37 in the third, along with a number of puerperae during the first week.

In all subjects, the following assays were carried out: total serum bilirubin, according to Jendrassik ([20]) (values expressed as mg/100 ml serum); alkaline phosphatase according to Bessey ([21]) (values expressed as U.K.A./100 ml); serum leucineaminepeptidase according to Rutenberg ([22]) (values expressed as mU/ml); and serum-glutamin traspeptidase according to Szasz ([23]) (values expressed as mU/ml).

The control group was made up of 20 women, not pregnant but fecund. Student's « t » test was used for statistical analysis of the data.

Testing was carried out on 9 placenta treated in the following manner: a piece of placenta tissue was immediately after birth and finely chopped in cold physiological solution (0°C) in order to release blood content, then homogenized in ULTRA-TURRAX (Mod. Typ. 18/23; Speed: U/min 20.000) and centrifuged at 71.000 × g.

PHA, γ-GT and LAP assays were carried out on supernatant. Results are expressed as enzymatic activity/g wet weight.

RESULTS

Fig. 1 shows results obtained with control subjects and with women at various months of pregnancy and in the first 2 weeks of puerperium. Part A reports bilirubin values, wich do not change significantly during pregnancy. Part B lists alkaline phosphatase values, wich increase during the second trimester and reach maximum levels during the third and in the first week of puerperium: a marked increase in comparision with controls and women in the first trimester of pregnancy. Part C reports values for leucineaminepeptidase, which follows the same patterns as alkaline phosphatase, i.e. it increases remarkably in the 3rd period and remains high during the first week of puerperium, while unlike alkaline phosphatase, it undergoes no statistically significant change during the second week.

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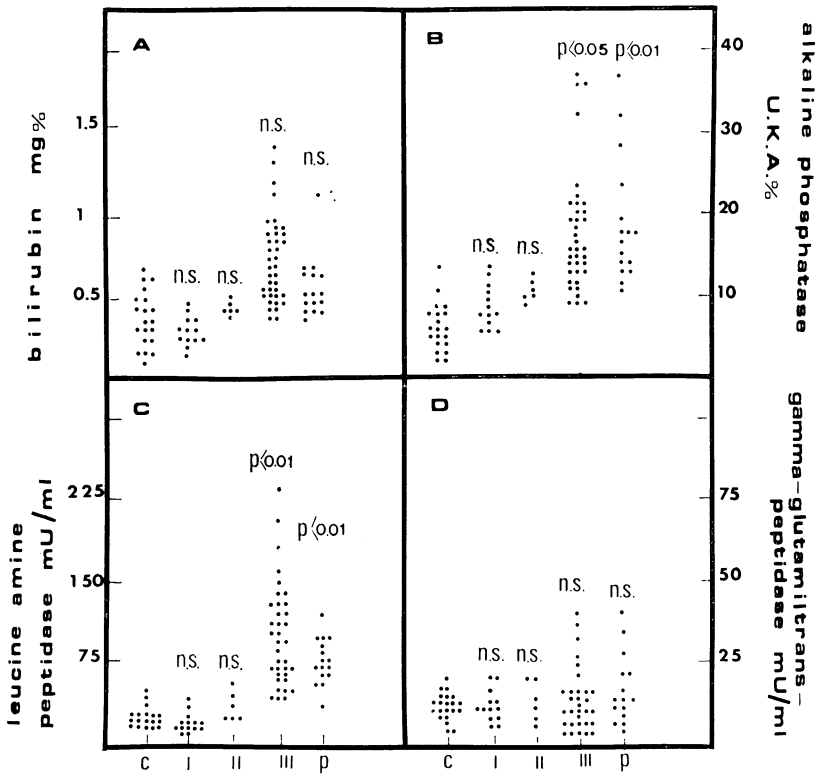

FIG. 1 - Shows the results of serum bilirubin, serum alkaline phosphatase serum leucineaminepeptidase in control subjects and in women at various stages of pregnancy. Par A reports the values of bilirubin expressed as mg/100 ml of serum; Part B reports the values of alkaline phosphatase expressed as U.K.A./100 ml of serum; Part C reports the values of leucineaminepeptidase expressed as mU/ml; Part D reports the values of γ-glutamiltranspeptidase expressed as mU/ml. Statistical analyses are reported where indicated.

Finally, γ-GT values are shown in part D. This enzymes shows no statistically significant alteration in any case, irrespective of the period of pregnancy.

Results obtained on placenta tissue are reported in Fig. 2. It is evident that PHA has the highest value: 2952±990 U.K.A./g wet weight, LAP 153.75±62.5 mU/g wet weight, while the method used for γ-GT showed no activity at all.

DISCUSSION

The present study, involving the three most important enzymes of cholestasis in pregnancy, demonstrates that two of them change irrespective of serum bilirubin, wich remains normal.

Interesting results were obtained concerning the behaviour of cholestasis enzymes. Like other authors ([16,17,18,19]) we have observed an increase in alkaline phosphatase and leucineaminepeptidase during the 3rd period of pregnancy, wich persists during the first week of puerperium. This increase is known be due to enzymes originating from placenta syncytiotrophoblast ([24]), an observation definitely established for alkaline phosphatase by the presence of a thermostable frac-

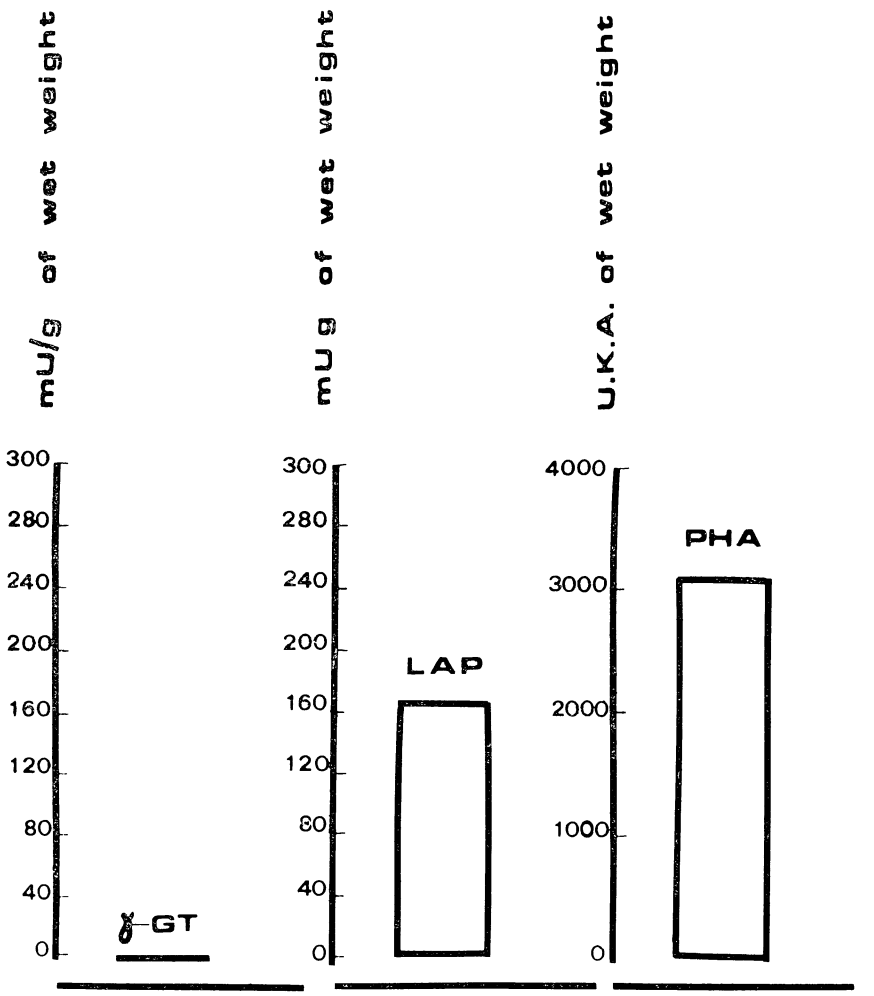

FIG. 2 - Shows the levels of placental alkaline phosphatase, leucineaminepeptidase and γ-glutamiltranspeptidase. Value are expressed as enzymatic activity/g of wet weight.

tion in the serum of pregnant women identical to that isolated from the placenta.

Data obtained on the behaviour of γ-glutamiltranspeptidase are especially relevant. In fact, this enzyme considered by some authors ([1, 3, 25]) to be the most sensitive in indicating cholestasis, even if limited to small areas of hepatic parenchyma, shows no variation during pregnancy.

Differences found in cholestasis enzymes in serum are dependent on their content in placenta tissue, with PHA having the highest values and, as has been seen, being the enzyme wich already shows an increase in the first period of the second trimester, reaching the highest of all cholestasis enzymes in serum. The absence of γ-GT in placental tissue explains the lack of increase in this enzyme in serum. These results suggest that the value of γ-GT in serum is the only index of liver cholestasis during pregnancy.

Clinical Experimental Obst. & Gynecology
Vol. III, 1-4, 1976 pp. 66-73

SUMMARY

In the present report, cholestasis enzymes have been observed during pregnancy, with study made of the three most important enzymes of cholestasis in serum: alkaline phosphatase (PHA), leucine amine peptidase (LAP), γ-glutamil transpeptidase (γ-GT).

In accordance with previous data, alkaline phosphatase and leucine amine peptidase levels were found to increase during the 3rd trimester of pregnancy, remaining elevated during the first week of puerperium, while no increase was observed in γ-glutamil transpeptidase in patients during pregnancy. The above changes in serum concentration of enzyne activity were all statistically calculated.

This study of cholestasis enzymes indicates the present of high concentrations, of PHA and LAP placenta tissue, with an absence of γ-GT. On the basis of these results, it is suggested that value of γ-GT in serum is the only index of cholestasis liver during pregnancy.

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Our experience in Monitoring pregnancy and delivery

by

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The decrease of the perinatal mortality rate is conditioned by the possibility of an early diagnosis of states of acute and chronic fetal destress, which can manifest themselves during pregnancy or labor.

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« Presentation to the VIII National Congress of the Yugoslav Society of Obstetric ». October 7-9, 1976.