

# SERUM LEUCINE AMINOPEPTIDASE ACTIVITY IN THE OBSTETRICAL AND GYNECOLOGICAL DISORDERS

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*Serum leucine aminopeptidase activity increases gradually with the gestation period, but not strikingly high enough during the first trimester to serve as a test for early pregnancy. In trophoblastic disease, particularly in hydatidiform mole, there is no definite elevation of serum leucine aminopeptidase activity. In ectopic gestation, fetal death and abruptio placentae, serum leucine aminopeptidase activity is markedly depressed. The probable mechanism of this phenomenon is recounted. The serum leucine aminopeptidase activity in cord blood is slightly elevated, but still lower than that of corresponding maternal blood. The possibility that serum leucine aminopeptidase is transmissible through the "placental barrier" is proposed. No significant serum leucine aminopeptidase deviation is found among the gynecological disorders, either neoplastic or non-neoplastic.*

## Introduction

The rise in serum leucine aminopeptidase (SLAP) activity in pregnant women was first noted by Green et al.<sup>10</sup> It has been confirmed by others:<sup>1, 3, 8, 12, 15</sup> and levels in abnormal pregnancy have been evaluated.<sup>1, 3, 12, 14, 15</sup> However, the mechanism of SLAP fluctuation during pregnancy is unknown. Leucine aminopeptidase, a proteolytic enzyme needed in the terminal digestion of L-leucyl peptides, is found in the mucosa of the small intestine and in pancreatic extracts,<sup>1</sup> in erythrocytes,<sup>2</sup> in blood vessel walls,<sup>11</sup> and in the placenta,<sup>15</sup> as well as in the uterus and the vagina.<sup>13</sup> The function of leucine aminopeptidase in the blood is unknown, and it has been found in the post-albumin and  $\alpha$ -globulin fractions of normal human serum.<sup>7</sup> Smith et al.<sup>16</sup> have also identified leucine aminopeptidase in the  $\alpha$ -globulin fraction of normal

serum and in the  $\alpha_2$ -globulin fraction of serum from pregnant women in the third trimester. In animal experiments, Chen et al.<sup>6</sup> found that the liver leucine aminopeptidase in rats decreased after protein depletion and increased after protein repletion. Further investigations of SLAP in hepato-biliary-pancreatic diseases revealed an increase in SLAP in association with conditions affecting the liver parenchymal tissue,<sup>1</sup> though it does not merit adoption as a differential diagnostic test.<sup>4</sup>

Further evaluation of SLAP in obstetrical and gynecological disorders will be of interest, particularly regarding 1) the value of SLAP detection in early diagnosis of pregnancy; 2) difference of SLAP activity among normal and abnormal pregnancies, especially in trophoblastic disorders; and 3) SLAP activity in uterine cervical carcinoma and other gynecological disorders.

## MATERIAL AND METHOD

### Material:

Normal non-pregnant blood specimens were collected from healthy student nurses, 20 to 22 years old. The obstetrical groups, both normal and abnormal.

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were made up of prenatal clinic patients and obstetrical ward patients in the Provincial Taipei Hospital; and gynecological specimens were collected from gynecological ward patients in the same hospital. Venous blood obtained from the cubital vein was allowed to clot in room temperature and centrifuged. The serum was stored under  $-20^{\circ}\text{C}$  and examined within a week.

### Method:

The method of SLAP determination was adopted from Goldberg, Pineda and Ruttenburg's,<sup>2</sup> except the final product was read on an Ito Colorimeter with 580 mu filter. The chemical reagents used were reagent grade.

The unit used in this experiment is the direct reading of optical density (x 1000) in this instrument without further calculation. One unit in this experiment approximately corresponds to six units in Goldberg's work.

## RESULT

### Normal Pregnancy:

In normal pregnancy, SLAP activity increases gradually, attains its highest value at term and falls again after delivery (Fig. 1). Statistic evaluation by the t-test revealed a markedly significant difference among the first, second and third trimesters, and post-partum period, but no significant difference between normal non-pregnant and the first trimester group (Table 1). After delivery, the SLAP level falls to half its value in the third trimester.

### Abnormal Pregnancy:

The SLAP level in trophoblastic disorders, particularly in hydatidiform mole, shows no significant deviation from normal pregnancy of corresponding duration (Table 2). Ectopic gestation and abruptio placentae differ from corresponding normal pregnant groups. This may be explained as a hemodilution effect after massive bleeding, although definite evidence of hemodilution was not identified in every case examined.

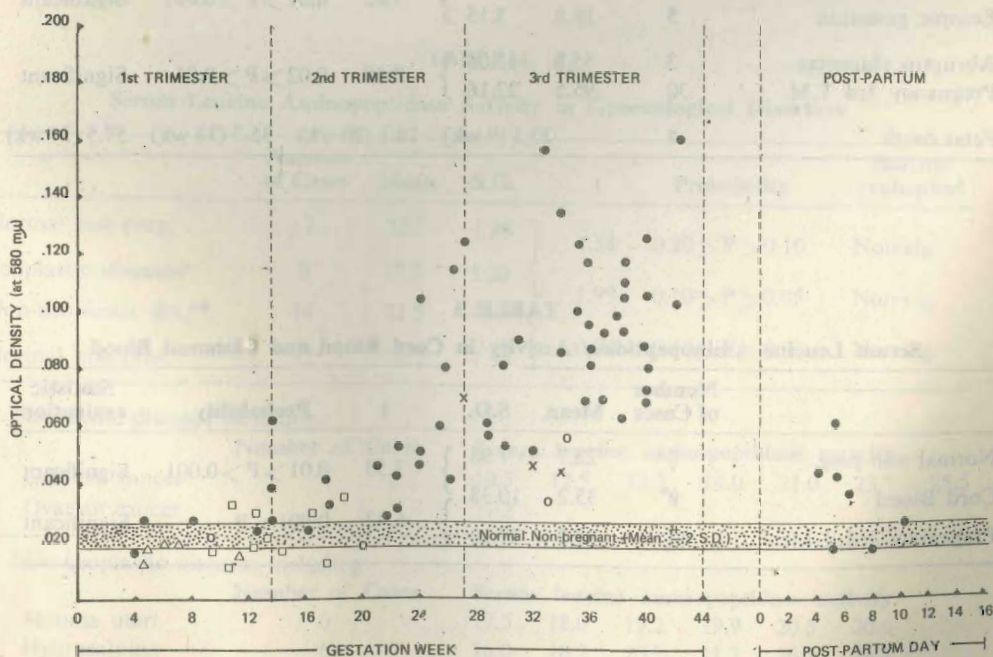


FIGURE 1 SERUM LEUCINE AMINOPEPTIDASE ACTIVITY IN PREGNANCY

● : Normal Pregnancy, ○ : Fetal Death, x : Abruptio Placentae,  
△ : Ectopic Gestation, □ : Hydatidiform Mole.

**TABLE 1**  
Serum Leucine Aminopeptidase Activity in Normal Pregnancy

	Number of Cases	Mean	S.D.*	t	Probability	Statistic evaluation
Normal non-preg.	7	22.7	1.98	1.54	0.20 > P > 0.10	Non-sig.
Pregnancy 1st T.M.**	7	31.3	14.82			
Pregnancy 2nd T.M.	16	60.5	48.08	2.19	0.05 > P > 0.02	Significant
Pregnancy 3rd T.M.	30	95.5	27.16			
Post-partum 4th day	4	36.4	10.51	3.06	0.01 > P > 0.001	Significant
Post-partum 8th day	2	22.4				

\* S.D. : Standard Deviation

\*\* T.M. : Trimester

**TABLE 2**  
Serum Leucine Aminopeptidase Activity in Abnormal Pregnancy

	Number of Cases	Mean	S.D.	t	Probability	Statistic evaluation
Hydatidiform mole	10	23.4	8.50	0.44	0.70 > P > 0.60	Non-sig.
Pregnancy 1st T.M.	7	31.4	14.82			
Ectopic gestation	5	16.8	3.15	3.62	0.01 > P > 0.001	Significant
Abruptio placentae	3	55.8	15.08			
Pregnancy 3rd T.M.	30	95.5	27.16	2.48	0.02 > P > 0.01	Significant
Fetal death	4	20.3 (9 wk)	18.1 (20 wk)			

**TABLE 3**  
Serum Leucine Aminopeptidase Activity in Cord Blood and Maternal Blood

	Number of Cases	Mean	S.D.	t	Probability	Statistic evaluation
Normal non-preg.	7	22.7	1.98	3.53	0.01 > P > 0.001	Significant
Cord Blood	9 <sup>b</sup>	35.2	10.38			
Pregnancy 3rd T.M.	30	95.5	27.16	6.42	0.001 > P	Significant

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The number of cases of fetal death is too small to offer grounds for a definite conclusion, but the SLAP activity seemed to be somewhat lower than normal levels at the comparable period of gestation.

**Cord Blood:**

The activity of SLAP in the cord blood of normal pregnancy is significantly lower than that of the third trimester group, but slightly higher than that of the normal non-pregnant group (Table 3).

**Gynecological Disorders:**

There was no significant difference in SLAP activity among the normal non-pregnant group, the neoplastic group and the non-neoplastic group of gynecological disorders (Table 4). Even for individual disorders, such as myoma uteri, hydrosalpinx, cervical polyp and ovarian cyst, there was no obvious difference. The small number of cases, however, rules out an absolute judgment.

**COMMENT**

It is well documented in the literature<sup>1, 3, 8, 10, 12, 15</sup> that SLAP activity increases during pregnancy. The results in this experiment as well as the results of Arst,<sup>1</sup> Siegel,<sup>15</sup> and Lewis,<sup>12</sup> show that SLAP activity increases gradually with the gestation period; in most cases, the levels during the first trimester do not show significant deviation from the normal non-pregnant value. Therefore, SLAP activity cannot serve as a test for diagnosis of early pregnancy. The highest level of SLAP comes at term and decreases sharply soon after delivery, to as low as half the value of the third trimester within a few days.

In trophoblastic disorders, particularly hydatidiform mole, SLAP activity is not significantly different from the normal gestation group. This was also demonstrated by Bressler and Forsyth<sup>3</sup> and Lewis.<sup>12</sup> SLAP activity can scarcely be considered to have any diagnostic value in trophoblastic disorders, though Bressler and Forsyth<sup>3</sup> emphasize

**TABLE 4**  
Serum Leucine Aminopeptidase Activity in Gynecological Disorders

	Number of Cases	Mean	S.D.	t	Probability	Statistic evaluation
Normal non-preg.	7	22.7	1.98	1.58	0.20 > P > 0.10	Non-sig.
Neoplastic diseases*	8	17.5	5.30			
Non-neoplastic dis.**	14	21.5	4.11			
Normal non-preg.	7	22.7	1.98	0.90	0.40 > P > 0.03	Non-sig.

\* Neoplastic diseases including:

	Number of Cases	Serum leucine aminopeptidase activity						
Cervical cancer	7	10.5	12.5	13.7	14.0	21.0	23.7	25.5
Ovarian cancer	1	21.2						

\*\* Non-neoplastic diseases including:

	Number of Cases	Serum leucine aminopeptidase activity						
Myoma uteri	6	17.5	18.0	19.2	19.9	20.5	20.6	
Hydrosalpinx	6	16.0	18.2	20.2	21.2	26.2	26.5	
Cervical polyp	1	26.0						
Ovarian cyst	1	31.0						

its diagnostic merit in hydatidiform mole if levels persist within the normal range after two months of gestation. In ectopic gestation and abruptio placentae, the results in this experiment showed a lower level of SLAP, perhaps explainable by a hemodilution effect after the acute massive bleeding that frequently accompanies these conditions. The lower level of SLAP in cases of pregnancy with a dead fetus, may be the result of placental dysfunction, if the placenta indeed plays a part in SLAP activity as described by Siegel,<sup>15</sup> as well as by Sciarra and Burress<sup>14</sup> in cases of twin pregnancy. However, it is difficult to account for the elevation of this enzyme in a missed abortion, reported by Arst,<sup>1</sup> if the placenta does play a role in SLAP activity. In toxemic patients, there is no demonstrable difference.<sup>15</sup>

In the cord blood of normal pregnancy, SLAP activity was higher than in the first trimester group in this experiment, contrary to previous investigations;<sup>1, 3</sup> while it was lower than that in the third trimester group. Therefore, SLAP may be able to cross the "placental barrier", though evidently not freely.

No significant difference in SLAP activity was found among cases of the above-mentioned gynecological disorders in this experiment. Even in the neo-

plastic diseases, there was little evidence of SLAP change, though Goldberg and Ruttenburg<sup>8</sup> noted its elevation in metastatic cancer, and Burston<sup>5</sup> found aminopeptidase activity in the stroma adjacent to the tumor by histochemical study.

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