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# New Rapid Test for Antepartum Assessment of Fetal Well-being

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**Abstract :** *Maternal perception of sound-provoked fetal movement test was studied on 2115 occasions in 1740 women with obstetric or medical antenatal risk factors after 26 weeks gestation. The response was compared with a nonstress test (NST) performed immediately after a three-second vibroacoustic stimulation with an electronic artificial larynx. A positive response to sound stimulation, recorded as a fetal movement by the mother, occurred on 2095 occasions (99.1%) and was accompanied by a reactive NST on 2071 occasions; giving a specificity of 99.7% and a negative predictive value of 98.8%. An inconclusive or negative response to sound (0.9%) had a sensitivity of 38.4% and a positive predictive value for a nonreactive NST of 75.0%. Results of sound-provoked fetal movement test and NST, performed within a week of delivery, in 1732 women were compared with fetal outcome. The maternal perception of sound-provoked fetal movement test had better specificity (99.5% vs 98.4%), positive predictive value (65.0% vs 35.0%) for poor fetal outcome than the NST, although its sensitivity (48.1% vs 51.8%) and negative predictive value (99.1% vs 99.2%) were slightly lower. However, the accuracy of this new rapid test for predicting fetal outcome is higher than the NST (98.8% vs 97.7%). Maternal perception of sound-provoked fetal movement test may suffice as an inexpensive and simple method of evaluating antepartum fetal well-being in risk situations. (Thai J Obstet Gynaecol 1992;4: 77-84.)*

**Key words :** fetal well-being, antepartum assessment, vibroacoustic stimulation, maternal perception, fetal movement

Ability to evaluate fetal condition is of major importance to those who provide health care for pregnant women. Several testing methods are presently used in antepartum assessment of fetal well-being. In Thailand, fetal movement counting and nonstress

tests (NST) are the common initial tests performed to assess fetal health. However, fetal movement charts are not very reliable and the NST is not widely performed especially in district hospitals or primary health care centres due to the cost of the machines.

Therefore, a new method which is simple and inexpensive to evaluate fetal well-being should be sought.

Fetal ability to respond to sound vibration has long been recognized and vibroacoustic stimulation of the fetus with an electronic artificial larynx has gained considerable attention<sup>(1-5)</sup>. Ultrasound studies have shown that fetal response to sound stimulation is analogous to the newborn startle reflex. The startle reaction includes blink response, head aversion, arm movements and leg extension and is mostly felt by the mother as a pronounced fetal kick or movement<sup>(6)</sup>. It has been suggested that assessment of this generalized paroxysmal fetal reaction could be a way to assess fetal neurological status<sup>(7)</sup>. Therefore, maternal perception of sound-provoked fetal movements might be used to assess fetal well-being.

The aim of this prospective study was to assess the reliability and possible applications of this test in high risk pregnancies. Maternal perception of sound-provoked fetal movement test was compared with the NST and with fetal outcome.

### **Materials and Methods**

Maternal perception of sound-provoked fetal movement test was studied at the Department of Obstetrics and Gynaecology, Chulalongkorn University Hospital, Thailand, from April 1990 to March 1992. All patients with obstetric or medical antenatal risk factors after 26 weeks ges-

tation, needing objective assessment of fetal well-being by NST, were recruited. Informed written consents were obtained after explanation of the test procedure to the patients. All patients knew that they were supposed to feel fetal movements during stimulation.

The vibroacoustic stimulation test was performed immediately before a conventional NST.

### *Vibroacoustic stimulation*

The test procedure was as follows. The patient was placed in a semireclining position. An electronic artificial larynx (EAL Model 146, Corometric Medical System, Connecticut, USA) was placed on the maternal abdomen over the position of the fetal head and vibroacoustic stimulation was applied for 3 seconds. An average of sound pressure levels of this device at 1 metre in air is 82dB with the fundamental frequency of 80 Hz and the harmonics range of 20-9000 Hz. A kick or fetal movement immediately following the vibroacoustic stimulation was considered a positive response (a normal test). If the patient did not feel any movements within 5 seconds, stimulation was repeated twice within 30 seconds. Fetal movements occurring 5 seconds or more after application of the stimulus were construed as spontaneous and not considered a normal test. If the woman did not feel fetal movements or was not sure, the test was considered negative or nonresponsive (an

abnormal test).

The test result was tabulated before the NST was performed.

The NST was performed immediately after the vibroacoustic stimulation with Fetal Monitor FM 4L (Sonic Aid, Chichester, UK) or Fetal monitor 145 (Corometrics, Connecticut, USA).

The NST was assessed by one of the authors (YT) without any knowledge of the result of the vibroacoustic stimulation test.

The NST was considered normal or reactive if 2 episodes of fetal heart rate accelerations of 15 beats above the baseline lasting for more than 15 seconds occurred in a 20 minutes window of the NST. If this criteria of reactive NST was not achieved, the NST was continued for another 20 minutes. The NST was considered abnormal or nonreactive if criteria for reactive could not be elicited even after extension of the test period to 40 minutes. Further obstetric management was based on the clinical situation and other investigation findings.

Results of the maternal perception of sound-provoked fetal movement test were related to results of the NST and both tests were related to perinatal outcome. Perinatal outcome was considered poor when there was perinatal death, a 5-minute Apgar score of less than 7, heavily meconium-stained amniotic fluid or admission to the neonatal intensive care unit.

Sensitivity, specificity, positive

predictive value and negative predictive value, and accuracy of the test were calculated.

## Results

During the study period 1740 high risk patients were recruited. Table 1 shows the antenatal risk factors in these patients. Of the total population 0.2% were 26-32 weeks, 8.3% were 33-37 weeks, 79.3% were 38-41 weeks, and the remaining 12.2% were over 42 weeks. Vibroacoustic stimulation and NST were performed on 2115 occasions in the study groups. On 20 occasions (0.9%) the response to sound was negative. Table 2 shows results of the maternal perception of sound-provoked fetal movement tests and the NSTs. Of the 2095 mothers who felt fetal movement, 2071 (98.8%) had a reactive NST, whereas, 24 (1.2%) had a nonreactive NST. Of the 20 mothers who felt no fetal movement, 15 (75.0%) had nonreactive NSTs. Sensitivity, specificity,

Table 1 Antepartum risk factors

Risk factors	No. of patients	%
Poor weight gain	548	31.5
Reduced fetal movements	293	16.8
Postterm ( $\geq$ 42 wk)	206	11.8
Pre-eclampsia	145	8.3
Suspected growth retardation	89	5.2
Antepartum hemorrhage	31	1.8
Others (poor obstetric history, diabetes, postdate, etc.)	428	24.6
<b>Total</b>	<b>1740</b>	<b>100</b>

positive predictive value and negative predictive value of the maternal perception of sound-provoked fetal movement tests compared to the NSTs are shown in Table 2. The accuracy of this test compared to the NST was 98.6%.

From the study population, 1732 patients had both tests performed within a week of delivery. Fetal outcome of these women was compared with the results of maternal perception of sound-provoked fetal movement

tests and NSTs. Twenty-seven fetuses were considered poor outcome namely, 9 perinatal deaths, 14 with heavily meconium-stained amniotic fluid, 2 cases of fetal distress in labour, and 2 cases admitted to the neonatal intensive care unit. Table 3 shows the results of maternal perception of sound-provoked fetal movement tests in relation to fetal outcome. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the maternal

**Table 2** Results of paired maternal perception of sound-provoked fetal movement (SPFM) tests and nonstress tests (NSTs)

Result of SPFM	No.	Result of NSTs	
		Reactive	Non-reactive
Positive	2095	2071	24
Negative	20	5	15

Sensitivity 38.4%, Negative predictive value 98.8%,  
 Specificity 99.7%, Accuracy 98.6%,  
 Positive predictive value 75.0%.

**Table 3** Results of maternal perception of sound-provoked fetal movement (SPFM) tests performed within a week of delivery in relation to fetal outcomes

Result of SPFM	No.	Fetal outcomes	
		Poor	Good
Positive	1712	14	1698
Negative	20	13	7

Sensitivity 48.1%, Negative predictive value 99.1%,  
 Specificity 99.5%, Accuracy 98.8%,  
 Positive predictive value 65.0%.

**Table 4** Results of nonstress tests (NSTs) performed within a week of delivery in relation to fetal outcomes

Result of NSTs	No.	Fetal outcomes	
		Poor	Good
Non-reactive	40	14	26
Reactive	1692	13	1679

Sensitivity 51.8%, Negative predictive value 99.2%,  
Specificity 98.4%, Accuracy 97.7%,  
Positive predictive value 35.0%.

**Table 5** Outcome of patients who had no maternal perception of sound-provoked fetal movements and a non-reactive nonstress test

Case	Antenatal risk factors	GA (wk)	Mode of delivery	BW (g)	Final outcomes
1	Reduced fetal movements	26	NVD	1450	Hydrops, stillbirth
2	Pre-eclampsia	35	C/S	1200	Trisomy 18, NND
3	Suspected IUGR	35	NVD	1900	Trisomy 18, NND
4	Reduced fetal movements	36	NVD	2000	Trisomy 18, NND
5	Reduced fetal movements	41	C/S	2450	IUGR, alive and well
6	Postterm	42	F/E	2630	Alive and well
7	Poor weight gain	41	C/S	3150	Alive and well
8	Reduced fetal movement	41	C/S	3300	Heavily meconium, alive and well
9	Suspected IUGR	39	C/S	1810	IUGR, alive and well
10	Postterm	42	C/S	3000	Alive and well
11	Chronic ITP	35	C/S	2200	NND
12	Suspected IUGR	36	NVD	1300	NND
13	Suspected IUGR	38	NVD	1800	NND, Trisomy 18
14	Suspected IUGR	36	NVD	1500	NND
15	Suspected IUGR	36	C/S	900	NND

GA = Gestational age, BW = Birth weight, NVD = Normal vaginal delivery, C/S = Caesarean section, NND = Neonatal death, IUGR = Intrauterine growth retardation, ITP = Immune thrombocytopenia.

perception of sound-provoked fetal movement test to predict poor fetal outcome were 48.1%, 99.5%, 65.0%, 99.1%, and 98.8%, respectively.

Table 4 compares fetal outcome in patients with reactive and nonreactive NSTs. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the conventional NST to predict poor fetal outcome were 51.8%, 98.4%, 35.0%, 99.2%, and 97.75%, respectively.

Table 5 provides details of fetal outcome in 15 cases when there was no maternal perception of sound-provoked fetal movement and a nonreactive NST. The results were poor with one stillbirth of a hydrops infant and 8 neonatal deaths (4 were aneuploid infants). Of the 6 survivors, 5 (cases 5, 7, 8, 9, 10) had ominous NSTs with clinical suspicion of fetal compromise necessitating emergency caesarean section; two (cases 5, 9) were growth retarded fetuses. Case 6 had a nonreactive NST with oligohydramnios; induced labour resulted in vaginal delivery of an infant in good condition.

## Discussion

Fetal ability to respond consistently to vibroacoustic stimulation with movements has been documented previously<sup>(2, 4-6)</sup>. Gelman et al<sup>(2)</sup> have reported increases in the number of fetal body movements in response to sound stimulation. A fetal eye-blink response to vibroacoustic stimulation

was demonstrated by Birnholz and Benacerraf<sup>(8)</sup>. Divon et al<sup>(7)</sup> studied the fetal startle reflex at EAL stimulation and suggested that assessment of this generalized paroxysmal fetal reaction could be a way to assess fetal neurological status. The startle response involves marked movement of both trunk and limbs and is a more vigorous movement than a spontaneous fetal movement. Therefore, it can be more easily recognized by the mother, giving a high perception rate as in our study and in 2 previous reports<sup>(9, 10)</sup>. It is possible that, unlike healthy fetuses, compromised fetuses might not react to vibroacoustic stimulation with startle movements. If that is so, then a positive response to sound stimulation could obviate the need for an NST. Our study found that maternal perception of sound-provoked fetal movement, when correlated with the NST, has high specificity and negative predictive value which means that when fetal movements are felt, NST is almost always reactive.

When both tests were compared for fetal outcome, the NST has slightly better sensitivity to identify fetuses who are in jeopardy than maternal perception of sound-provoked fetal movement test. However, both tests have high specificity and negative predictive value. This finding implies that whenever the mother feels fetal movements during sound stimulation, the fetus is usually in good health. When movements are not felt, other standard tests should be performed, i.e. NST or biophysical pro-

file. Therefore, maternal perception of the sound-provoked fetal movement test may serve as a first line screening test before requesting the NST.

The NST with the adjunctive use of fetal acoustic stimulation to reduce the number of nonreactive test has become an accepted investigation for antepartum fetal health<sup>(3)</sup>. Arulkumaran et al<sup>(10)</sup> found a low incidence of nonreactive NST (3.4%) after application of the stimulation once or twice and suggested that the nonreactive NST rate can be reduced further by an appropriately timed third stimulus. Because of growing concern for fetal health, more tests are being requested, with more demands on time and personnel, and greater cost in performing the test.

According to our study, we suggest that if the mother feels no fetal movements during the stimulus and the NST is nonreactive, structural abnormalities and chromosomal abnormality in the fetus should be ruled out.

The advantages of maternal perception of the sound-provoked fetal movement test are 1) highly economical, 2) little expertise needed to interpret the results, 3) considerable reduction in time, 4) better predictability of fetal health than fetal heart rate auscultation, and 5) can be performed anywhere even by the mother. The guideline using maternal perception of sound-provoked fetal movement test for assessment of fetal health in a primary health care setting where NST is not available is pro-

posed. In an antenatal clinic when a high risk pregnancy is identified, the mother should be referred to a tertiary care centre or monitoring of the fetal health continued by using daily fetal movement chart and maternal perception of sound-provoked fetal movement test every second or third day. If the mother does not feel fetal movements during the stimulation, she should be referred.

The safety of vibroacoustic stimulation has been questioned. Two studies looked into the problem of hearing loss following in utero exposure to acoustic stimulation. One tested 40 babies 1-2 days of age<sup>(11)</sup> and the other tested 465 children at the age of 4 years<sup>(12)</sup>. Neither have shown any evidence of auditory damage. There is no attenuation of the sound produced by the devices when sound pressure level is measured in utero using a hydrophone<sup>(13)</sup>. The lack of damage must be due to the short duration of exposure during the fetal acoustic stimulation test or to reduced ciliary movement due to acoustic impedance of the amniotic fluid. It is known that cochlea ciliary damage is less in chick embryos exposed to noise compared to hatched chicks<sup>(14)</sup>. Therefore, it would seem that the potential clinical benefit outweighs any theoretic risk currently associated with the technique.

In conclusion, maternal perception of the sound-provoked fetal movement test is a simple and inexpensive method for evaluating fetal well-being. An obvious disadvantage

is the lack of objective recording. Like the NST, this test seems to be a good predictor of fetal health, but the absence of maternal perception of fetal movement does not always indicate fetal compromise, further evaluation is needed. This test may be used as a first line screening test in busy antenatal clinics before requesting the NST. In addition, this clinical application may be helpful for assessment of fetal health at risk, in primary health care settings.

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# Relationship Between Time of Birth and Perinatal Death Ramathibodi Hospital : 1981 - 1989

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**Abstract :** *A 9-year retrospective review of the relationship between time of birth and perinatal death at the Department of Obstetrics and Gynaecology between January 1, 1981 and December 31, 1989. There were 63518 births with a total of 427 perinatal deaths, of which 222 deaths were stillbirths and 205 were neonatal deaths. The perinatal mortality rate was 6.72 per 1000 births. PMR were 6.85 and 6.34 for babies born on weekdays and weekends, respectively and the PMR for babies born between 16.01-08.00 hr was 8.20 higher than that between 08.01-16.00 hr, which was 5.60 per 1000 births. The incidence of preventable death from asphyxia and specific conditions also showed an increase during 16.01-08.00 hr. In order to reduce PMR further, improvement in intrapartum care and management between 16.01-08.00 hr should be reviewed. (Thai J Obstet Gynaecol 1992;4:85-88.)*

**Key words :** time of birth, perinatal death

Perinatal mortality rate (PMR) is an indicator of the quality of obstetric and neonatal cares. It also reflects the respective maternal and child health. The problems encountered when trying to improve PMR other than socio-demographic make-up of patients are shortages of personnel, facilities, equipment and maldistribution of these factors which may be related to time of birth. The objective of this study was to identify rates and causes of perinatal death at different time of

birth. It is hoped that the findings will help to improve the quality of obstetric and neonatal care services and at the same time reduce further perinatal mortality and morbidity.

## Materials and Methods

Data was collected from a summary of delivery records of patients delivering single births at Ramathibodi Hospital between January 1, 1981 and December 31, 1989. The World

Health Organization's definition of perinatal mortality is used<sup>(1)</sup>. It defines perinatal mortality as a total of all stillbirths occurring at or over 28 weeks of gestation and neonatal deaths during the first week. The perinatal mortality rate is defined as the number of perinatal deaths expressed as a proportion of 1000 total births occurring in the same area at the same time. Wigglesworth's classification for perinatal deaths is used in this analysis<sup>(2)</sup>. The time of birth was grouped into 2 categories, for babies born between 08.01-16.00 hr or between 16.01-08.00 hr due to official and non-official working hours.

## Results

During the period of study, there were 63518 births with a total of 427 perinatal deaths, of which 222 deaths were stillbirths and 205 were neonatal deaths. The perinatal mortality rate was 6.72 per 1000 births (Table 1). PMR were 6.85 and 6.34 per 1000 births for babies born on weekdays and weekends, respectively (Table 2) and the PMR for babies born between 16.01-08.00 hr was 8.20 per 1000 births, higher than that between 08.01-16.00 hr, which was 5.60 per 1000 births (Table 3). Incidence of preventable death from asphyxia and specific conditions such as hypertensive disorders in pregnancy, antepartum hemorrhage, group B streptococcal infection, and meconium aspiration syndrome were also shown to increase during 16.01-08.00 hr (Table 4).

**Table 1** Perinatal mortality of singleton births, Ramathibodi Hospital, 1981 - 1989

Years	Births	SB	NND	PMR
1981	6526	23	26	7.51
1982	6698	22	23	6.72
1983	6759	25	26	7.55
1984	6649	26	23	7.37
1985	6780	23	18	6.05
1986	7495	28	24	6.94
1987	7222	24	24	6.65
1988	7750	26	21	6.06
1989	7640	25	20	5.89
Total	63518	222	205	6.72

SB = Stillbirths  
NND = Neonatal deaths  
PMR = Perinatal mortality rate

**Table 2** PMR for babies born on weekday and weekend, Ramathibodi Hospital, 1981 - 1989

Day of births	Births	SB	NND	PMR
Weekday	47429	168	157	6.85
Weekend	16089	54	48	6.34
Total	63518	222	205	6.72

**Table 3** PMR for babies born during 08.01 - 16.00 hr and 16.01 - 08.00 hr, Ramathibodi Hospital, 1981 - 1989

Time of births	Births	SB	NND	PMR
08.01 - 16.00	36064	100	102	5.60
16.01 - 08.00	27454	122	103	8.20
Total	63518	222	205	6.72

**Table 4** PMB by causes of death for babies born during 08.01 - 16.00 hr and 16.01 - 08.00 hr, Ramathibodi Hospital, 1981 - 1989

Causes of death	Time of births			
	08.01 - 16.00		16.01 - 08.00	
	PND (n = 36064)	PMR	PND	PMR
Congenital malformations	85	2.36	90	3.29
Maceration	67	1.86	64	2.33
Prematurity	14	0.39	14	0.51
Asphyxia	27	0.75	36	1.31
Specific condition	9	0.25	21	0.76
<b>Total</b>	<b>202</b>	<b>5.60</b>	<b>225</b>	<b>8.20</b>

## Discussion

The perinatal mortality rate at Ramathibodi Hospital has declined dramatically from 14.0 per 1000 births in 1975 to 6.9 per 1000 births in 1989<sup>(3,4)</sup>. When comparing the perinatal mortality rate with other institutions, it was the lowest one<sup>(5-7)</sup>. The cause for this decline is mainly due to continuous patient care during antepartum, intrapartum and postpartum including risk factors screening<sup>(8)</sup>, active management<sup>(9)</sup>, labour graphic records<sup>(10)</sup>, and the use of tocolytic drugs<sup>(4)</sup>. The main reduction in perinatal mortality rate is due to the reduction in neonatal deaths, whereas, the stillbirth rate remain fairly constant. It will need further investigation to find a way to reduce the stillbirth rate but this will be even more difficult and will require a more costly input. Other factors that might influence perinatal mortality apart from the ob-

stetrical care are socio-economic, physical and cultural environment of the patient, the method of data collection and time of birth. According to the time of birth, many studies have shown that perinatal death was high during the weekend and between evening and early morning<sup>(11-15)</sup>. From this study the result was the same only between 16.01-08.00 hr compared to 08.01-16.00 hr but between weekdays and weekends the result was not significantly different. It was noted that the incidence of preventable death from asphyxia and specific conditions was shown to have increased during 16.01-08.00 hr. In order to reduce PMR further, improvement of intrapartum care and management during the non-official working hours between 16.01-08.00 hr should be reviewed. In this way the perinatal mortality rate can be reduced as well as preventable deaths.

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# Study of Immunoreactive 8-Arginine Vasopressin in Human Plasma During Pregnancy and at Delivery : Utilization of a Highly Sensitive Radioimmunoassay with a Reversed Phase C18 Silica Column

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**Abstract :** *Changes in plasma concentration of immunoreactive(IR) 8-arginine vasopressin (AVP) during pregnancy and at delivery were examined using a highly sensitive radioimmunoassay (RIA). The following results were obtained : (1) The maternal plasma concentrations of IR-AVP gradually decreased during pregnancy and reached a plateau after week 28 up to delivery. From week 28, the plasma concentrations of IR-AVP were significantly lower than those before week 15 ( $2.4 \pm 0.36$  pg/ml). Maternal plasma IR-AVP levels at normal vaginal delivery did not differ from those at delivery by elective cesarean section. (2) The umbilical arterial plasma concentrations of IR-AVP at vaginal delivery ( $390 \pm 60.6$  pg/ml), which were significantly higher than those of umbilical venous plasma ( $224 \pm 34.1$  pg/ml), were markedly higher than at delivery by cesarean section ( $14.1 \pm 9.1$  pg/ml). (3) The fact that the concentrations of IR-AVP in the umbilical arterial plasma at delivery, in cases of asphyxia ( $505 \pm 74.1$  pg/ml), were significantly higher than those at normal delivery ( $300 \pm 13.3$  pg/ml) is noteworthy. These results suggest that : (1) In the mother, AVP acts as an antidiuretic hormone to maintain the homeostasis of physiologically increased total body water and decreased body tonicity, associated with pregnancy. (2) In the fetus, AVP acts as a stress hormone to maintain the homeostasis of cardiovascular and metabolic systems, which are subjected to the influence of labour. (Thai J Obstet Gynaecol 1993;4:89-98.)*

**Key words :** 8-arginine vasopressin (AVP), pregnancy, normal vaginal delivery, elective cesarean section, asphyxia

8-Arginine vasopressin or antidiuretic hormone is a nonapeptide secreted from the posterior lobe of the pituitary gland, which mainly exerts

an antidiuretic effect through the V2 receptor in low blood concentrations<sup>(1)</sup>, and a vasoconstrictive effect through the V1 receptor at high concentrations in human beings<sup>(2)</sup>.

It is well known that AVP regulates water metabolism and its secretion is also accelerated at the time of stress<sup>(3)</sup>. In order to evaluate fetomaternal AVP function, we established a highly sensitive radioimmunoassay (RIA) system and measured immunoreactive (IR-) AVP in maternal plasma during pregnancy, when a prominent physiological change occurs in water metabolism, and fetal umbilical plasma at delivery, when a high level of stress would be estimated.

## Materials and Methods

### *Subjects and collection of samples*

Blood samples were collected from patients who visited or were admitted to the Osaka University Hospital. They all gave their informed consent to participate in this study. The subjects examined consisted of 4 groups as follows.

Group I : non-pregnant group (12 samples),

Group II : normal pregnancy group (30 samples),

Group III : normal vaginal delivery group (34 samples),

Group III was divided into two further subgroups, which were;

Group III-(a) : non-asphyxia group (27 samples),

Group III-(b) : asphyxia group

(7 samples).

Group IV : elective cesarean section group.

In Groups I and II, blood was withdrawn in the sitting position at 9:00-12:00 am. In Groups III and IV, blood samples were obtained 3 minutes after delivery. In the vaginal delivery group III, labour started spontaneously and progressed to vaginal delivery. In the cesarean section group IV, mothers did not eat or drink from 9:00 pm on the day before the operation and received 500 ml of saline intravenously before operation. Spinal anesthesia was used during operation and no severe hypotension was observed. In all cases, blood loss at delivery was less than 500 ml. In the asphyxia group, III-(b), none of the 1 minute Apgar score of newborn infants was more than 7 and cord pH was below 7.20, and in non-asphyxia, III-(a), the 1 minute Apgar score was more than 8 in all cases. In group III-(b), the mean Apgar score was  $6.1 \pm 0.8$ , which was significantly lower than that of group, III-(a). There was no significant difference in other parameters, such as, average maternal age, parity, height, weight, blood pressure or neonatal body weight (Table 1).

All samples were mixed with peptidase inhibitor (EDTA-2Na 1.5 mg/ml of blood) in an ice-chilled plastic test tube, the plasma separated and stored at  $-20^{\circ}\text{C}$  until extraction.

Statistical comparisons were made by Mann-Whitney U test and the student t-test, and the significance

**Table 1** Comparisons of various parameters of umbilical arterial plasma IR-AVP (mean±S.E.M.)  
(\*; <0.05 vs (3), \*\*; P<0.01 vs (3))

		maternal age(years)	fetal body weight(kg)	gestational age(weeks)	mean 1min apgar score	UA-AVP (Pg/ml)
(3)	(a) (n=27)	32.3±5.5	3.065±228	39.4±1.3	8.8±0.4	300±43.3
	(b) (n=7)	30.7±4.2	3.066±547	39.2±1.2	* 6.1±0.8	* 505±74.1
(4) (n=10)		36.0±2.2	3.260±276	38.0±0.8	8.9±0.2	** 14.0±9.1

(3); normal vaginal delivery group

(a) non-asphyxia group

(b) asphyxia group

(4) elective cesarean section group

of difference was  $p < 0.05$ .

### Measurement of AVP

#### (a) Antiserum

Antiserum was kindly provided by the Mitsubishi Yuka Science Co, Ltd.<sup>(4)</sup> It was produced by immunizing New Zealand white rabbits with synthetic 8-AVP and the thyroglobulin complex coupled with carbodiimide. Antiserum was used at the final dilution of 100000.

#### (b) Iodination of AVP

Standard AVP was purchased from the Peptide Institute, Osaka, Japan and used for iodination. Iodination was carried out by the chloramine T method<sup>(5)</sup>. Labelled-AVP was purified on a Sephadex G-25 fine column

(0.7x20 cm, Pharmacia Fine Chemicals, Upsala, Sweden) and developed with 0.1 mol/l acetic acid.

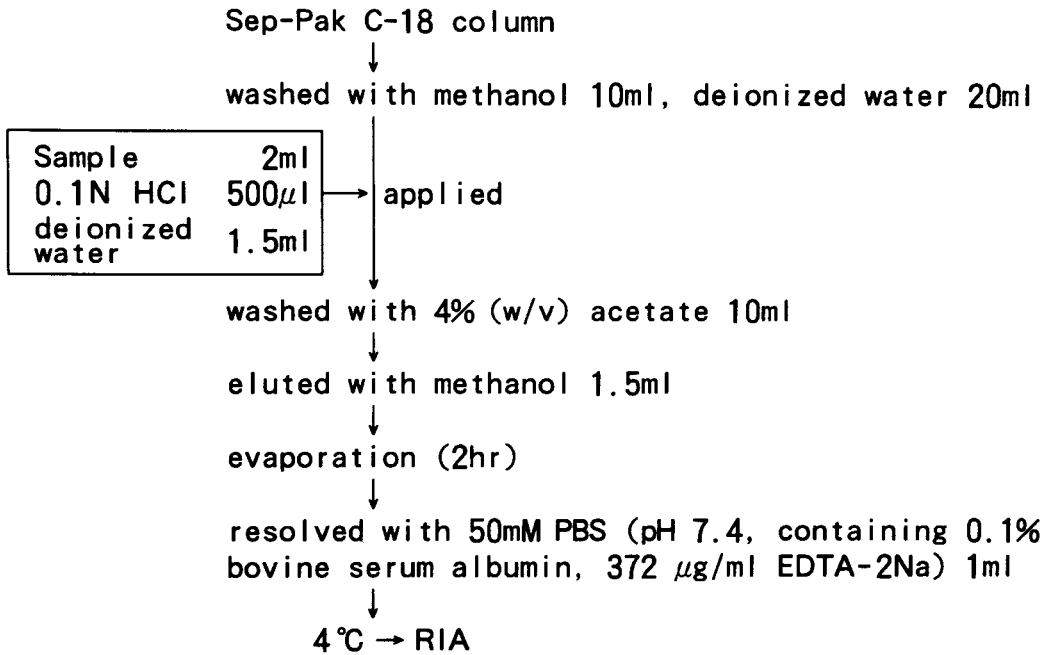
#### (c) Extraction of AVP from plasma

Octadecylsilane cartridge (Sep-Pak C18, Waters Associates, Milford, MA, USA) was used for extraction as indicated in Fig. 1.

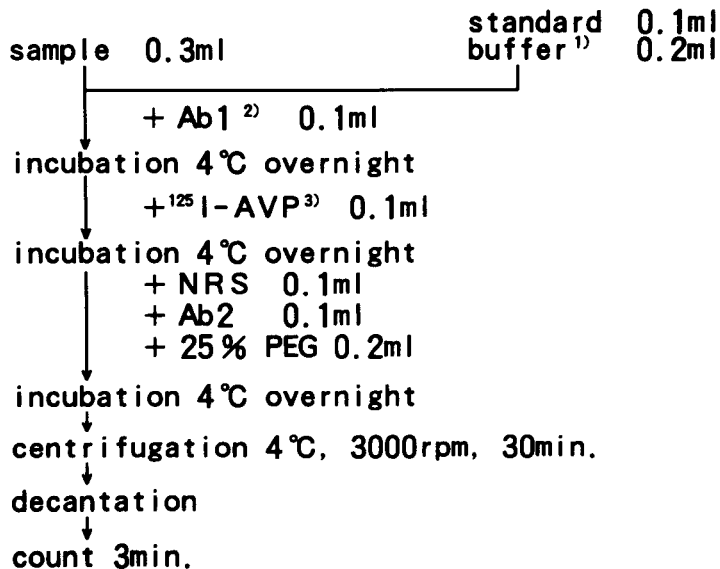
#### (d) Radioimmunoassay of AVP

The extracted material (300  $\mu$ l) in phosphate buffer and 100  $\mu$ l anti-AVP in 1% (v/v) normal rabbit serum were mixed in a test tube and incubated overnight at 4° C and labelled-AVP (2500 cpm/100  $\mu$ l) was then added. Free and bound radioactivity was by the addition of 100  $\mu$ l of a second antibody (anti-rabbit IgG sheep serum; 1:20), 100  $\mu$ l of NRS

## Figure 1 Extraction



## Figure 2 <Radioimmunoassay>



1) assay buffer : 0.1 M PB (0.01% NaN<sub>2</sub>) containing 0.1% BSA PH 7.4

2) Ab1 : anti-AVP rabbit serum (titer 1 : 100,000 final)  
AVP (Ferring A.B.) -porcine thyroglobulin conjugated was injected into female rabbits

3) <sup>125</sup>I-AVP : 2500 cpm/ml

and 200  $\mu$ l of 25% PEG. After overnight incubation at 4° C, the tubes were centrifuged and the radioactivity in the precipitate was measured (Fig. 2).

The minimal detectable level of AVP was 0.05 pg/tube and the inter- and intra- assay coefficients of variation were < 7.85% and 8.24%, respectively (n=5). The mean recovery rate, determined by addition of synthetic AVP was 87.1%. The cross-reactivity of antiserum with lysine vasopressin, oxytocin and vasotocin was 100%, < 0.05% and < 0.4%, respectively.

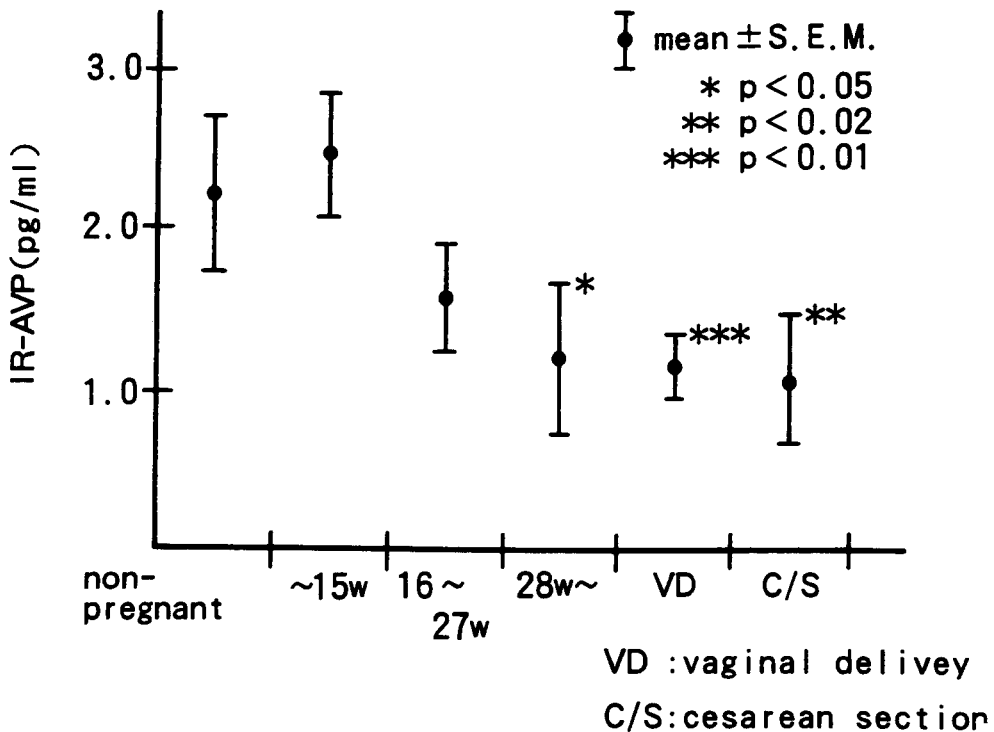
### Results

#### *Maternal plasma IR-AVP during pregnancy and at delivery*

The maternal plasma concentrations of IR-AVP gradually decreased during pregnancy and reached a plateau after week 28 up to delivery. From week 28, the plasma concentrations of IR-AVP (mean  $\pm$  SEM) were significantly lower than the one before at delivery by elective cesarean section (Fig. 3).

Figure 3 : Maternal plasma IR-AVP levels during pregnancy and at delivery (mean  $\pm$  S.E.M.)

(\* : P<0.05, \* ; P<0.02, \*\*\* < 0.01, VS. pregnancy ~ 15w)



### Maternal and umbilical cord plasma IR-AVP at delivery

Umbilical cord plasma IR-AVP levels were significantly higher than that of maternal plasma and the difference was pronounced in the vaginal delivery group. The umbilical arterial plasma concentrations of IR-AVP ( $390 \pm 60.6$  pg/ml,  $n=34$ ) were significantly higher than those of umbilical venous plasma ( $224 \pm 34.1$  pg/ml,  $n=29$ ) ( $p<0.05$ ). On the other hand, there was no significant difference in maternal plasma between vaginal delivery and elective cesarean section groups, but in both umbilical venous and arterial plasma, the IR-AVP concentrations in the vaginal delivery group was markedly higher than those in the elective cesarean group ( $p<0.001$ ) (Fig. 4).

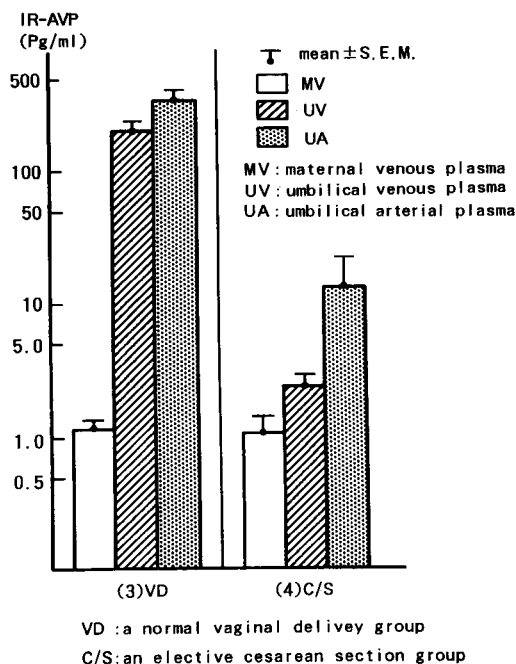
### Umbilical arterial plasma IR-AVP in case of neonatal asphyxia

It was noteworthy that the umbilical arterial plasma at delivery in cases of asphyxia ( $505 \pm 74.1$  pg/ml,  $n=7$ ) was significantly higher than that at normal delivery ( $300 \pm 13.3$  pg/ml,  $n=27$ ) (Table 1).

### Discussion

There have been several reports concerning the relationship between plasma AVP level and maternal plasma osmotic pressure<sup>(6)</sup>, or fetal hypoxia<sup>(7)</sup>, from either the maternal or fetal point of view. However, there

Figure 4. Maternal and umbilical cord plasma IR-AVP levels at delivery (mean  $\pm$  S.E.M.)



are few reports concerning AVP from these points of view in both. Besides, the sensitivity of the measurement of plasma AVP has not always been satisfactory because the AVP concentration in human plasma is quite low.

We have established a highly sensitive RIA system to evaluate fetomaternal AVP function with different modes of delivery and fetal asphyxia from both maternal and fetal points of view.

A striking increase in water metabolism and a mild decrease of plasma osmotic pressure occurs physiologically in pregnancy. Renal plasma flow increases about 45% and cardiac output also increases about 40% in the first trimester and reaches

a plateau which is maintained up to week 30<sup>(8)</sup>. Plasma osmotic pressure after 10 weeks pregnancy decreases to 10 mOsm/kg less than in the non-pregnant status (280-282 mOsm/kg, nonpregnant;  $273 \pm 0.5$  mOsm/kg, pregnant;  $277.0 \pm 0.5$  mOsm/kg, delivery), and maintains this plateau level up to delivery<sup>(9)</sup>. Coinciding with this, the plasma osmotic pressure threshold of AVP secretion from the posterior lobe pituitary decreases<sup>(6)</sup>.

Our finding that the plasma concentration of IR-AVP is significantly lower than that before week 15 suggests that AVP plays an important role in maintaining increased volume of maternal blood circulation and decreased osmotic pressure during pregnancy.

In a recent study, AVP RNA expression in the hypothalamo-neurophyseal system during pregnancy did not differ from that in the non-pregnant<sup>(10)</sup>, but the plasma vasopressinase (cystine amino peptidase) level and inactivation of AVP in the placenta increased after the third trimester of pregnancy<sup>(11)</sup>. These results support the conjecture that an increase of AVP metabolic rate causes a decrease of plasma AVP concentration and contributes to the promotion of water metabolism during pregnancy. Our observation that maternal plasma IR-AVP levels at normal vaginal delivery did not differ from those at delivery by cesarean section suggest that stress such as labour pain, does not necessarily reach the threshold of accelerating AVP secretion in pregnant

women without serious complications, such as PIH or massive hemorrhage at delivery.

Human natriuretic peptide (hANP), which has a reverse effect against AVP of natriuresis and decreases blood pressure by relaxing vascular smooth muscle, increases during pregnancy<sup>(12)</sup>, and inhibits vasopressin secretion<sup>(13)</sup>. These facts suggest that this hormone will have a relationship to AVP, on water metabolism, during pregnancy.

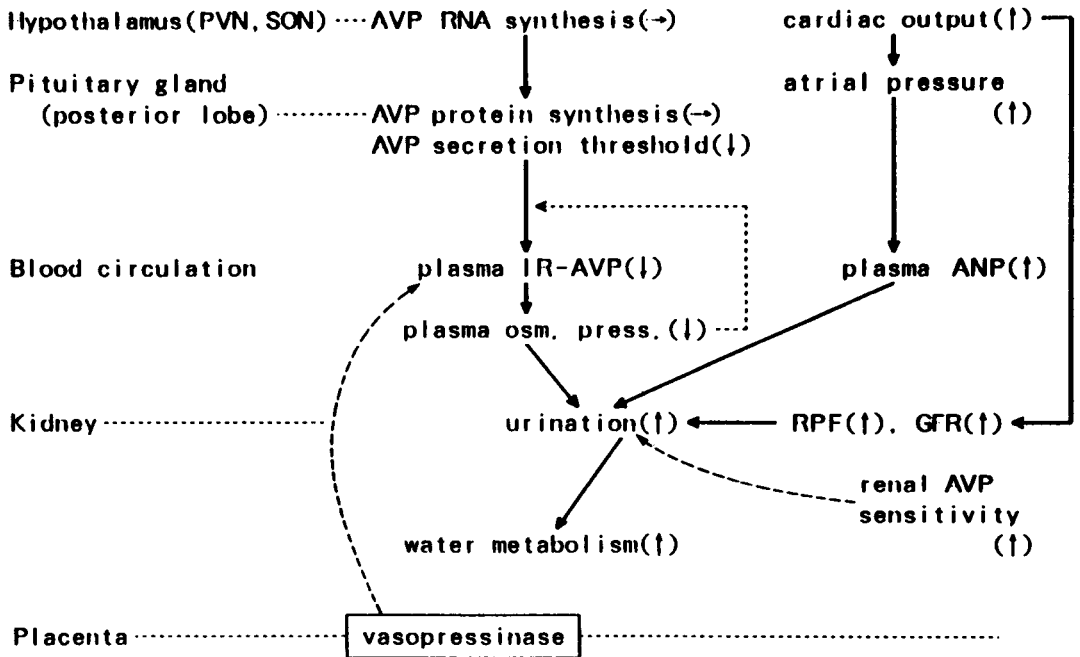
AVP plays a role in the fetal cardiovascular response to stress, such as hypoxia or hypotension, as a consequence of hemorrhage. It is postulated that there is no shift of AVP between fetus and the mother as the placenta has a large amount of vasopressinase and inactivates AVP<sup>(11)</sup>. Accordingly, the high concentration of IR-AVP in the umbilical cord plasma, is of fetal production, so that, the fetus itself secretes AVP in response to the stress of labour, in order to maintain cardiovascular homeostasis. In asphyxia, further secretion of fetal AVP would be accelerated, and contribute to the redistribution of blood flow and the selective supply of oxygen and nutrition to the important organs, such as, brain, heart or adrenal glands.

In addition to epinephrine, norepinephrine and AVP, corticotropin releasing hormone (CRH) is being investigated recently as a stress hormone. CRH as well as AVP directly effects the anterior lobe of the pituitary gland and regulates ACTH secre-

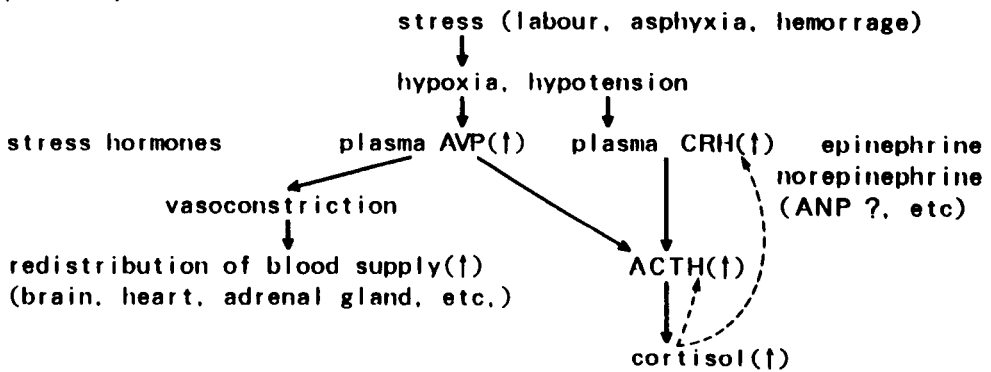
Figure 5.

**HYPOTHESIS OF FETO-MATERNAL AVP FUNCTION DURING PREGNANCY AND DELIVERY**

< MOTHER >



< FETUS >



————→ acceleration  
 .....→ supression

(↑) increase  
 (→) stable  
 (↓) decrease

tion. We have previously reported that umbilical cord plasma IR-CRH also increases in cases of asphyxia<sup>(14)</sup>. Taking these facts into consideration, AVP may play an important role in the fetus as a stress hormone.

In other reports, AVP was shown to accelerate hANP secretion<sup>(15)</sup>, and the umbilical arterial plasma concentration of IR-hANP at vaginal delivery was significantly higher than the venous plasma<sup>(16)</sup>.

In summary, there must be a complex interaction among several stress hormones during pregnancy and AVP may play a key role in maintaining the homeostasis of cardiovascular and metabolic systems (Fig. 5).

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# Determination of Serum Lipid Levels During Mid-Trimester Hypertonic Saline Solution Induced Abortion

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**Abstract :** *Lipid metabolism modifications during pregnancy are strictly correlated with changes of the hormonal factors which regulate it. Serum lipid levels rise during the progression of gestation and reach the peak at the end of pregnancy. Although these changes are reversible, the possible influence of elevated serum lipids on atherosclerotic and ischemic cardiovascular disease as well as biliary tract lithiasis development is still unresolved. The aim of this study was to investigate interrelationship between serum lipids during mid-trimester hypertonic saline solution induced abortion. Blood samples were taken from the cubital vein of 30 primigravid women, without any endocrine and metabolic disorders, ages 15-40, admitted for the mid-trimester pregnancy abortion, four times: I) before instillation intraamnion ultrasonographically guided hypertonic saline solution application (control), II) three hours after, III) in the active phase of abortion, and IV) twelve hours after the curettage. Quantitative assay was used for determination of total cholesterol, triglycerides, phospholipids, LDL and HDL, while apolipoprotein A1 and apolipoprotein B were determined by immunochemical methods. Three hours after instillation levels of cholesterol, phospholipids, HDL and apolipoprotein A1 were higher, while other lipids were lower, compared to the control group. During the abortion's active phase all lipid concentrations were higher, compared to the control ones, but only apolipoprotein B level was lower. Triglyceride was found to be on the same level as to that before the procedure. Twelve hours after curettage, serum lipid concentrations decreased, reaching control levels. Apolipoprotein A1 and apolipoprotein B were supposed to have a protective role against biliary tract disease development, while decreased proportions of LDL to HDL suggest that they are relevant to atherosclerosis development. (Thai J Obstet Gynaecol 1993;4:99-103.)*

**Key words :** hypertonic saline solution, mid-trimester pregnancy abortion, serum lipid levels

On the basis of bibliographic references and our own data, maternal hyperlipidemia at late gestation results from the juxtaposition of several fac-

tors: a) maternal hyperphagia and unmodified gut lipid absorption increasing chylomicron formation from dietary lipid, b) enhanced adipose

tissue lipolysis facilitating the availability to the liver of substrates for triglyceride synthesis, and c) reduced lipoprotein lipase activity in extrahepatic tissues, especially adipose tissue, which does not allow a triglyceride and other lipids removal proportional to their enhanced production<sup>(1)</sup>.

According to the literature data about half of the pregnancies are terminated by abortion. During only one year about 35-55 million abortions were performed in the world while 84000 of women died due to pregnancy interruption complications<sup>(2)</sup>. It is also well known that mid-trimester pregnancy abortion can be performed by hypertonic saline solution as well as by prostaglandin or mifepristone given intramuscularly<sup>(3)</sup>. Mid-trimester pregnancy abortion has twenty times higher morbidity and mortality risk compared to the first trimester one<sup>(4)</sup>.

Elevation of serum lipid levels during pregnancy is progressive and reversible<sup>(5,6)</sup>. Previous investigations confirmed that serum lipid concentrations rise during mid-trimester pregnancy abortion induced by prostaglandin and proposed that their investigation may be of use for the study of atherosclerotic and ischemic cardiovascular disease as well as for biliary tract lithiasis development. So, the aim of this research was to investigate serum lipid levels during mid-trimester pregnancy abortion induced by intraamnially application of hypertonic saline solution and to speculate their possible role in the pathogenesis

of those diseases.

## Materials and Methods

The study comprised of 40 primigravid women, without any endocrine or metabolic disorders, ages 15-40, admitted for mid-trimester pregnancy abortion for social reasons.

After the routine investigations on admission, gestational age was assessed by gynaecological and ultrasonographic examinations. Peripheral blood samples from the cubital vein were taken four times: before ultrasonographically guided intraamnially applied hypertonic saline solution instillation (I) (control group), three hours after that (II), in the active phase of abortion (III), and twelve hours after the placental expulsion and curettage (IV). The levels of total cholesterol, triglycerides, phospholipids, LDL and HDL were investigated by quantitative assays, while concentrations of apolipoprotein A1 and apolipoprotein B were determined by immunochemical methods. Obtained data were tested by variance analysis for attributive parameters.

## Results

Concentrations of cholesterol, phospholipids, HDL and apolipoprotein A1 were slightly higher three hours after application of hypertonic saline solution compared to the controls, while levels of other investigated lipids were lower, but not significantly ( $p > 0.05$ ) (Table 1).

**Table 1** Serum lipid levels during mid-trimester hypertonic saline induced abortion

	<i>before intervention</i>	<i>3 h after instillation</i>	<i>during abortion's active phase</i>	<i>12 h post abortion</i>
Cholesterol (mmol/l)	6.50 +/- 1.09	6.97 +/- 0.06	7.28 +/- 0.28	6.85 +/- 1.35
Triglycerides (mmol/l)	2.04 +/- 0.70	1.49 +/- 0.32	2.04 +/- 0.23	1.49 +/- 0.50
Phospholipides (mmol/l)	3.26 +/- 0.32	3.65 +/- 0.13	3.50 +/- 0.16	3.32 +/- 0.13
LDL (mmol/l)	3.57 +/- 1.06	3.38 +/- 0.30	3.73 +/- 0.21	3.16 +/- 0.38
HDL (mmol/l)	1.81 +/- 0.55	2.49 +/- 0.20	2.69 +/- 0.40	1.98 +/- 0.34
Apolipoprotein A1 (g/l)	1.92 +/- 0.17	2.15 +/- 0.07	2.26 +/- 0.11	1.95 +/- 0.04
Apolipoprotein B (g/l)	1.51 +/- 0.35	1.38 +/- 0.10	1.46 +/- 0.03	1.32 +/- 0.06

During the active phase of abortion all serum lipid levels were higher compared to the controls ( $p < 0.05$ ), while only apolipoproteins B were slightly lower. Triglyceride concentrations were found to be the same as those before instillation.

Twelve hours after the placental expulsion and curettage, serum lipids were decreased compared to the previous respective sample concentrations. Serum lipid levels in this postabortive phase are comparable to those before the abortive procedure initiation.

### Discussion

A significant alteration of maternal metabolism occurs during pregnancy. It seems certain that these changes are the result of fetomaternal interaction. This can be concluded from the fact that they are observed

only during the period when the products of conception coexist within the mother and are almost completely reversed after delivery<sup>(7)</sup>.

There is a relatively small number of investigations of serum lipid levels during mid-trimester pregnancy abortion. Changes of serum lipids during the abortion active phase is due to the stress effect on pituitary-adrenal axis, and elevation of ACTH and cortisol concentration in the serum<sup>(8)</sup>.

In healthy persons, lipid metabolism modifications are strictly correlated with changes of the hormonal factors which regulate it<sup>(9)</sup>. During progression of gestation there is a steady and significant increase of serum cholesterol levels and LDL lipoproteins, but also a decrease of HDL lipids<sup>(10)</sup>. Maximal serum lipid concentrations are registered between the 33rd and 36th week of gestation<sup>(5)</sup>.

Jimenez et al in 1988<sup>(6)</sup> found that HDL is in negative correlation with cholesterol and triglycerides during the second half of gestation. Our investigation confirmed significantly lower LDL to HDL levels after instillation. This finding may indicate a protective role of HDL in atherosclerosis and ischemic myocardial disease development, but biochemism of this protective mechanism is still unclear<sup>(11)</sup>.

In a detailed study of serum lipids during hypertonic saline solution induced abortion Sane et al in 1983<sup>(12)</sup> found that serum cholesterol levels rose in the abortion's active phase and dropped sharply after termination of the abortion, as did the concentrations of phospholipids and triglycerides. However, we found that triglycerides in the active phase of abortion were on the same level as those before instillation, showing a slightly decrease three hours after initiation of the procedure and twelve hours after the curettage, while cholesterol and phospholipids showed the same trend as those in the cited papers. Steady increase of serum cholesterol levels during gestation is due to a progressive concentration rise of LDL. Composition of these lipoproteins is changed and manifested in decreased ratio of cholesterol and apolipoprotein B<sup>(10)</sup>. This finding is not in correlation with estrogen and progesterone levels rise. If the content of biliary cholesterol is a reflection of the serum concentration of this lipid, bile may be more lithogenic during pregnancy<sup>(13)</sup>.

Investigating vascular disease risk factors, Carlton et al<sup>(14)</sup> proved that the increased proportion of LDL to HDL suggests that a person is exposed to an increased theoretical long term vascular risk. Phospholipids are very important for the metabolism of arachidonic acid, as a precursor of prostaglandins, prostacyclins and tromboxans<sup>(15)</sup>. Increase of serum phospholipid concentrations that we have found is due to degenerative and necrotic changes in feto-placental compartment. Apolipoprotein A1, a constitutive part of HDL and chylomicrons, stimulates hepatic lipoprotein lipase and is very important in cholesterol and HDL metabolism<sup>(16)</sup>. Clinical value of apolipoprotein A1 determination is still unresolved, but we found that its concentrations were almost the same after the abortion procedure was completed compared to those before the instillation. We must admit that, far from being clear, however, is our understanding of the underlying mechanisms. We propose that they have, besides an HDL, a protective role in atherosclerosis and ischemic myocardial disease as well as biliary tract lithiasis development. Zannis and Brsesloa<sup>(17)</sup> regarded the concentrations rise of apolipoprotein B to be due to LDL binding for their specific receptors. It was confirmed that elevated apolipoprotein B is more important for atherosclerotic changes of development in blood vessels than decreased concentrations of HDL<sup>(11)</sup>.

In conclusion one can say that, although apolipoprotein A1 and

apolipoprotein B were supposed to have a protective role against biliary tract diseases development and the decreased ratio LDL/HDL suggests their relevance to atherosclerosis commencement. Serum lipid levels require further investigations for elucidation of pathophysiological changes during pregnancy.

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## **8th Scientific Annual Meeting**

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# Mid-Trimester Termination of 51 Intact Pregnancies by Condom-Balloon Technique

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**Abstract :** *A total of 51 complicated intact pregnancies at Chiang Mai University Hospital which had indications for termination of pregnancy were accumulatively intervened and monitored. The interim evaluation has lately been carried out. All of them were between 13-28 weeks of gestation and terminated by extra-amniotic stimulation with condom-balloon and subsequent oxytocin augmentation. The mean age of all patients was 26.43 years (ranged 18-39 years) and the mean gestation was 18.63 weeks (ranged 13-28 weeks). The rates of success of termination within 24, 48, and 72 hours were 56.9, 84.3, and 92.2 % respectively. The average induction-abortion time (IA) was 23 hours 49 minutes, which is not significantly different when comparing primiparity and multiparity. Only 3 out of 51 (6.4%) needed surgical curettage due to incomplete expulsion. Only 3 cases developed fever but needed no intensive care. Blood loss was so minimal by close observation that this phenomenon should be substantiated. The result of this paper is quite impressive and strongly suggests that the use of condom-balloon for stimulation and termination of mid-trimester pregnancy is an appropriate procedure because of high efficacy, very minimal complications and it is not expensive. Further investigation and a wider scale of clinical monitoring are suggested. (Thai J Obstet Gynaecol 1993;4:105-110.)*

**Key words :** mid- trimester termination, extra-amniotic stimulation, condom-balloon

The conventional technique of therapeutic termination for early pregnancy by suction curettage is simple and safe. It is, however, indicated that surgical complications increase with the advancement of the gestational age<sup>(1)</sup>. Surgical evacuation and curettage is, therefore, not recommended when the uterus is over 16 weeks<sup>(2-3)</sup>. Intra-

amniotic instillation of hypertonic solution such as 20 % sodium chloride has commonly been used in late second trimester pregnancy. Complications, such as hypernatremia, can be a serious problem if hypertonic saline is incorrectly applied. Until lately, prostaglandins and analogues such as sulprostone have been proven to be effective

for second trimester pregnancy termination<sup>(3-5)</sup>. It is, however, indicated that the clinical implication of prostaglandins and derivatives in developing countries such as Thailand is still limited due to the very high expense and evidence of considerable side effects including nausea, vomiting, and diarrhea.

An earlier report of the new method by using condom-balloon technique for extra-amniotic stimulation of endogenous prostaglandin indicated that it is a highly effective method for termination of a dead fetus in utero and has minimal morbidity<sup>(6)</sup>. It is also much less expensive. At Maharaj Nakorn Chiang Mai Hospital, this technique is currently being used as the primary method of choice for termination of second trimester pregnancy both intact pregnancy and a dead fetus if there is no contraindication. The objective of this paper is interim evaluation of the application of the condom-balloon technique for intact mid-trimester pregnancy termination.

### **Materials and Methods**

A total of 51 cases of 13-28 weeks intact pregnancies which were relevant for termination at Maharaj Nakorn Chiang Mai Hospital from April 1985 to April 1992 were accumulatively monitored and evaluated. All of them were justified for therapeutic termination based upon the individual medical indication. All had no labour pain and had no contraindications including cervicitis, rupture of membranes, cho-

rioamnionitis, undiagnosed fever, and leakage of amniotic fluid. The clinical response and the events of the individual woman were recorded for subsequent evaluation.

### *Preparation of the condom-balloon apparatus*

The condom-balloon apparatus consists of one ordinary rubber urethral catheter of # 14-16, one standard male rubber condom, silk threads of # 3/0, and a metallic catheter guide. All of the above items can be sterilised by soaking in an antiseptic solution (Cidex) for 15 minutes. Under sterile conditions the condom sheath was put over the rubber catheter tip making the condom-balloon portion about 3.5 to 4.0 inches long by doubling ligatures with silk thread. It is very important to make sure that the lumen of the rubber catheter is still patent after ligation. The length of the catheter tip from the ligatures should be about 2 inches long to facilitate the application of the condom-balloon into the uterine cavity. The excessive portion of the condom sheath was then excised. The preparation procedure is illustrated in Fig. 1.

### *Technique of insertion of the condom-balloon*

Under sterile techniques, empty the air within the condom-balloon by deflation with an irrigation syringe otherwise it will be difficult during the application. Holding the anterior lip of

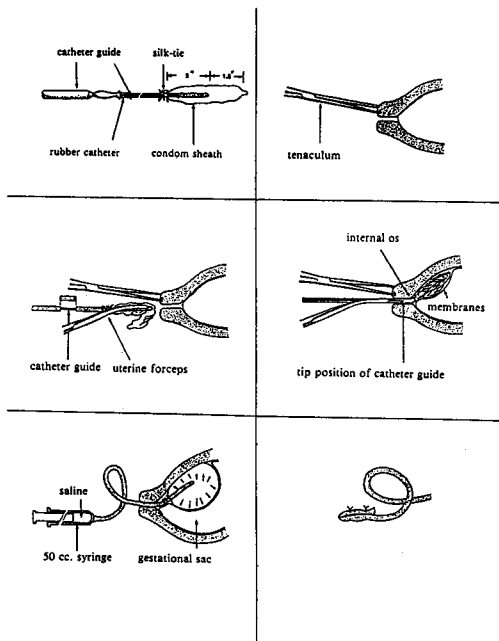


Fig.1 Condom-balloon technique.

the cervix with a tenaculum during gentle advancement of the condom-balloon apparatus into the cervical canal by using curved uterine forceps. The use of catheter guide is frequently recommended for easier application but be sure not to advance the tip of the catheter guide beyond the internal os in order to avoid accidental iatrogenic rupture of the amniotic sac. The balloon is gently advanced in any direction depending on its own freeness until the double knots of ligature are above the internal os and the entire condom-balloon is in the uterine cavity. The balloon is then inflated with normal saline according to the uterine size: 50-100 ml for 12-16 weeks, 100-150 for 16-19, 150-200 for 20-23, and 200-250

for 24-28 weeks respectively. The other end of the catheter was then clamped or tightly ligated with silk and be kept in the vagina for comfortability.

### Care after balloon insertion

Bed rest or relaxing activity is acceptable for the patients and waiting for spontaneous labour is advised. After labour has started, the patient is transferred to the labour room for oxytocin augmentation (not more than 10 mIU/ml). Drug or analgesia may be given depending on the individual pain threshold. The patient was observed and wait for the progress, spontaneous expulsion of the condom-balloon, and subsequent expulsion of the conceptus or delivery. All clinical events and steps were recorded for subsequent evaluation.

### Results

A total of 51 mid-trimester intact pregnancies were accumulatively terminated and monitored according to the various indications as shown in Table 1.

The average age of the 51 patients was  $26.43 \pm 5.2$  (ranged 18-39 years). Twenty eight out of 51 were primiparity. The mean gestational age was  $18.63 \pm 3.2$  weeks (ranged 13-28 weeks) and the uterine size by examination averaged about  $16.82 \pm 4.0$  weeks (ranged 12-28 weeks).

The accumulative rate of success for expulsion or delivery within 24,48 and 72 hours was 29 of 51 (56.9%), 43

**Table 1** Indications for therapeutic termination of intact pregnancies

Indications	Number
Maternal rubella	11
Hydrops fetalis and Hb Bart	9
Mental retardation	5
Heart disease	5
Severe pre-eclampsia	5
Rape victim	4
Fetal anomaly	4
Schizophrenia	3
Brain tumour	2
Leukemia	1
Lymphoma	1
Breast cancer	1
<b>Total</b>	<b>51</b>

There was no significant difference of the average IL time between primiparity (13 h 16 min) and multiparity (11 h 3 min) ( $p > .05$ ). The average IA time between primiparity (24 h 2 min) and multi-parity (22 h 58 min) was also not statistically different ( $p > .05$ ). Of the 47 successful terminations, 3 patients or 6.4% needed surgical curettage due to incomplete expulsion. It is noteworthy that 11 of 47 had spontaneous expulsion or delivery of the fetus within the intact amniotic sac.

Clinical complications were found in only 3 women, one had febrile morbidity over 38 ° C during retention of the condom-balloon within the

**Table 2** Percentage of patients by parity and time needed for induction

Parity	Induction-abortion time (IA) in hours and ( %)				
	<24	<48	<72	Failure	Total
0	16(57.1)	24(85.7)	27(96.4)	1(3.6)	28(100)
1	13(56.5)	19(82.6)	20(87.0)	3(13.0)	23(100)
<b>Total</b>	<b>29(56.9)</b>	<b>43(84.3)</b>	<b>47(92.2)</b>	<b>4(7.8)</b>	<b>51(100)</b>

of 51(84.3%), and 47 of 51 (92.2%) respectively as shown in Table 2. Four patients or 7.8% failed to be terminated within 72 h and needed subsequent induction by parenteral sulprostone. Of the successful terminations, the average induction-labour time (IL) was 12 h 20 min and induction-abortion time (IA) was 23 h 49 min.

uterus and the other two had fever on day 1 and day 2 post expulsion but none of them needed intensive care or prolonged hospitalization. In general cases of abortion, blood loss is among the common complications. From this interim evaluation, 4 cases or 8.5% were classified as scanty or minimal blood loss, 34 cases (72.3%) mild or

small amount of blood loss (<150 ml), and 9 cases (19.6%) moderate degree (150-500). There was, however, no severe blood loss or bleeding of more than 500 ml (Table 3).

**Table 3** The estimated blood loss of the condom-balloon technique

Degree	N	%
Scanty or minimal	4	8.5
Mild (< 150 ml)	34	72.3
Moderate (150-500 ml)	9	19.6
Severe (>500 ml)	-	-
<b>Total</b>	<b>51</b>	<b>100.0</b>

### Discussion

At Maharaj Nakorn Chiang Mai University Hospital, the condom-balloon technique has routinely been used as the primary procedure in the therapeutic termination of mid-trimester pregnancies for more than 10 years. The objective of this interim evaluation is to re-evaluate the clinical implication. Until lately, it has been demonstrated that it is highly effective for mid-trimester pregnancy termination without any serious complications or systemic adverse effects.

The mechanism of induction of labour by using the condom-balloon technique is hard to explain. It has been proven earlier that mechanical stimulation of the fetal membranes

results in prostaglandins production<sup>(7)</sup>. It is, therefore, possible that the extensive mechanical separation of the membranes and the decidua by the condom-balloon initiates the release of endogenous prostaglandin and results in subsequent uterine contraction. It may also induce biomedical changes in both tissues which contain large amounts of arachidonic acid that is the precursor of prostaglandins<sup>(8)</sup>. The labour induced by the condom-balloon somewhat mimics natural labour or labour which develops after the use of exogenous prostaglandins. The distinction of this new technique is that there is no problem of overstimulation leading to severe complications such as rupture of the uterus as seen from the use of parenteral prostaglandins.

On one hand, the direction for insertion of the condom-balloon apparatus is somehow automatically advanced in the direction of decidua vera and this phenomenon has been proven by ultrasonographic examination. In the long-term cumulative experience at this hospital, there was neither evidence of bleeding or abruption placentae. On the other hand, blood loss from this technique is surprisingly minimal. It is probably due to vasoconstrictive effect of the endogenous prostaglandins. However, keep in mind that any bleeding from the uterus noticeable during pregnancy is contraindication for application of the condom-balloon because it can be placenta previa.

The other interesting phenomena

of the condom-balloon technique is evidence that most of the cases experienced spontaneous complete expulsion and the considerable number of patients who had spontaneous deliveries with the fetus within the intact amniotic sac.

Unlike exogenous prostaglandins, the condom-balloon technique has no systemic adverse reaction, therefore, it is more appropriate for a complicated pregnancy, such as heart disease. The disadvantage of this technique is the long induction-interval that is theoretically subject to risk of infection. In the current setting, however, this is not considered a problem if contraindications have earlier been excluded.

In conclusion, this paper has shown that the condom-balloon technique for extra-amniotic stimulation of mid-trimester termination is highly effective and also has minimal morbidity. It is undoubtedly much less expensive and appropriate technology for developing countries.

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# Transvaginal Sonography in the Diagnosis of Ectopic Pregnancy

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**Abstract :** *To assess the usefulness of transvaginal sonography in diagnosing ectopic pregnancy, the medical records and ultrasonograms of 111 patients referred for transvaginal sonography with a clinical diagnosis of suspected ectopic pregnancy during a one-year period were reviewed. Of these patients, ectopic pregnancy was diagnosed in 37 women (33.33%), complete abortion in 16 women (14.42%), intrauterine pregnancy in 14 women (12.62 %) and corpus luteum cyst in 11 women (9.91 %). In each case of ectopic pregnancy in this series, at least one abnormal uterine, adnexal, or peritoneal finding was detected at transvaginal sonography. An extrauterine gestational sac with living embryo, allowing a definitive diagnosis, is seen in only 5.4 % of cases. Certain sonographic features such as an adnexal ring or nonspecific adnexal mass with intraperitoneal fluid are helpful in making the diagnosis of an ectopic pregnancy. Because of its improved resolution of uterine and adnexal structures, transvaginal sonography is recommended as a primary imaging modality for detailed evaluation of patients with suspected ectopic pregnancy. Meticulous transvaginal sonographic technique and a high index of suspicion will facilitate the diagnosis of ectopic pregnancy in most cases. (Thai J Obstet Gynaecol 1993;4:111-118.)*

**Key words :** transvaginal sonography, ectopic pregnancy

Despite advances in diagnosis made by the introduction of serum beta-subunit human chorionic gonadotropin determinations and transabdominal ultrasonography, ectopic gestations still present a major diagnostic challenge and remain the major cause of maternal mortality in the first trimester of pregnancy. The increased resolution of the transvaginally introduced high-frequency ultrasound transducer seems

to resolve this diagnostic problem. Transvaginal sonography has improved overall diagnosis in several significant ways. Intrauterine pregnancies are now reliably diagnosed at an even earlier stage in pregnancies than ever before. Ectopic pregnancy as well as other abnormal gestations can now be confirmed more frequently and earlier than ever before.

This study was initiated to in-

investigate the diagnostic value of transvaginal sonography as the sole investigation in the diagnosis and exclusion of ectopic pregnancy.

### Materials and Methods

The medical records and ultrasonograms of 111 patients referred for transvaginal sonography with a clinical diagnosis of suspected ectopic pregnancy at the Department of Obstetrics and Gynaecology, Chulalongkorn University, during the one-year period (beginning in January 1991) were reviewed. The equipment used in this study included Toshiba Model SSA-250A and Aloka Model SSD-680 to which a 5.0 MHz mechanical sector transvaginal transducer was attached.

The ultrasonographic data collected in each case included the following: the presence or absence of an

intrauterine gestational sac, fluid in the cul-de-sac, endometrial thickness, adnexal mass, or a gestational sac in an ectopic location. The endometrial thickness was assessed by obtaining a longitudinal section of the uterus and measuring the outer to outer thickness of the endometrium. An endometrial thickness > 10 mm was considered abnormal. All the patients were followed up after the ultrasound examination to ascertain the clinical outcome. These sonographic findings were analysed and correlated with clinical outcome.

### Results

Of the 111 patients referred for transvaginal sonography with a clinical diagnosis of suspected ectopic pregnancy, the final diagnosis and clinical characteristics of the 111 women studied are summarized in Table 1.

**Table 1** Final diagnosis in 111 women with suspected ectopic pregnancy

Final Diagnosis	Cases	%
Ectopic pregnancy	37	33.33
- unruptured ectopic pregnancy	26	23.42
- ruptured ectopic pregnancy	11	9.91
Normal intrauterine pregnancy	14	12.62
Blighted ovum and missed abortion	3	2.70
Complete abortion	16	14.42
Pelvic inflammatory disease	4	3.60
Ovarian cyst	3	2.70
Endometriotic cyst	6	5.41
Corpus luteum cyst with or without bleeding	11	9.91
No abnormality detected	12	10.81
Anovulation	4	3.60
Appendicitis	1	0.90

In the 37 cases of ectopic pregnancy diagnosed by transvaginal sonography and confirmed by laparoscopy and/or laparotomy, there were 26 patients with unruptured, and 11 patients with ruptured ectopic pregnancy. In each case of ectopic pregnancy, at least one abnormal uterine, adnexal and

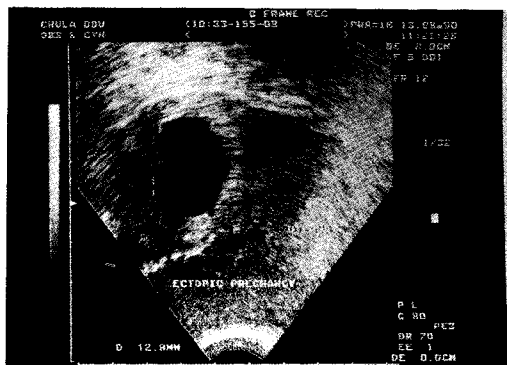
peritoneal findings detected at transvaginal sonography.

Table 2 summarizes the frequency of the sonographic features that were assessed. It was not uncommon for one patient to have more than one finding.

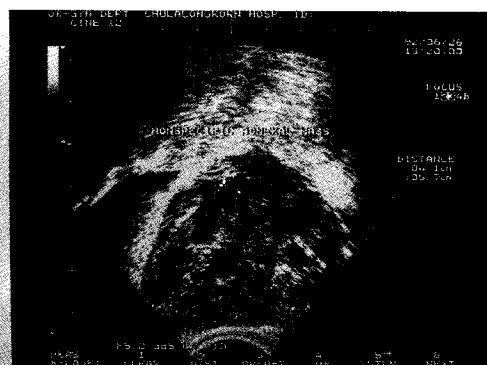
Table 3 shows the ultrasound

**Table 2** Findings from transvaginal sonography in 37 ectopic pregnancies

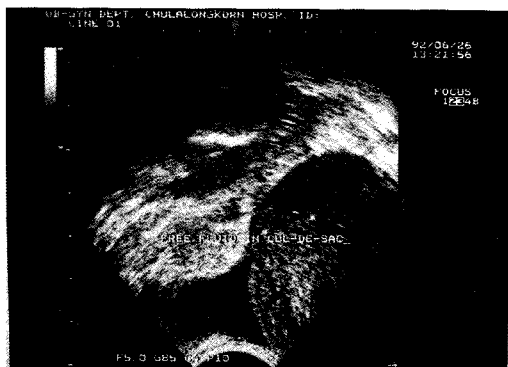
Findings	No. of cases (%)
<b>Uterus</b>	
: thickened endometrium (>10 mm)	6 (42.86 %)
: pseudosac	1 (7.14 %)
: absence of gestational sac	37 (100 %)
<b>Adnexae</b>	
: adnexal ring (Fig. 1)	11 (29.73 %)
-with living embryo	2 (5.41 %)
-with embryo or yolk sac	6 (16.22 %)
: nonspecific adnexal mass (Fig. 2)	30 (81.08 %)
<b>Cul-de-sac</b>	
: fluid in the cul-de-sac (Fig. 3)	22 (59.46 %)



**Fig. 1** Transvaginal sonogram shows the adnexal ring containing an embryo with heart motion.



**Fig. 2** Transvaginal sonogram shows nonspecific adnexal mass.



**Fig.3** Transvaginal sonogram shows fluid in the cul-de-sac.

nal sonography, which would demonstrate a normal gestational sac with a fetal pole either inside or outside the uterus. Unfortunately, the sonographic image is not always easy to interpret. Therefore, the primary role of ultrasound is limited to excluding this life-threatening condition by the demonstration of an intrauterine pregnancy<sup>(1)</sup>.

The vaginal approach provides better access to the pelvic organs and allows a clear view of the uterus and

**Table 3** Diagnostic accuracy of the sonographic features in the diagnosis of ectopic pregnancy

Ultrasound features	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Adnexal ring structure and alive embryo	5.40	100.00	100.00	67.89
Adnexal ring	29.73	95.95	78.57	73.20
Free fluid in the cul-de-sac	59.46	82.43	62.86	80.26
Endometrial thickness (> 10 mm)	46.15	72.00	46.15	72.00
Nonspecific adnexal mass	81.08	84.21	71.43	90.41

findings in the 111 women with suspected ectopic pregnancy, analysed in relation to diagnostic accuracy of the particular ultrasound feature investigated.

### Discussion

Previously, the diagnosis of ectopic pregnancy was confirmed or ruled out by employing transabdomi-

adnexae, with no need to fill the bladder. Excellent visualization of the endometrial cavity permits the detection of even a very early intrauterine pregnancy and clearly shows the other fluids in the cul-de-sac which can also be seen easily.

In each case of ectopic pregnancy in this series, at least one abnormal uterus, adnexal, or peritoneal finding was detected at transvaginal sonography as same as previously

published<sup>(2,3)</sup>. In our series, an adnexal mass or adnexal ring representative of the extrauterine gestation was detected with transvaginal sonography in all patients harboring an ectopic pregnancy. According to the varied clinical courses and pathological appearances of ectopic pregnancy with respect to viability (i.e. viable ectopic pregnancy, tubal rupture, or abortion of ectopic pregnancy and localization i.e. tube, ovary, or abdomen), the sonographic feature is variable.

The adnexal ring was documented in 29.7% of cases and with a live embryo in 5.4 % of cases. This proportion is lower than that reported by others<sup>(4,5)</sup>. Identification of an extrauterine gestational sac with a live embryo allows a definitive diagnosis of ectopic pregnancy, but was not commonly encountered. In our opinion, the yolk sac within the gestational sac also allows confirmatory diagnosis. The thick-walled ring without internal echoes, however, is not in itself a specific sign, because other adnexal processes such as hemorrhagic corpus luteum cysts can mimic this appearance.

A nonspecific adnexal mass was detected in 81.1 % of cases. Detection of a nonspecific adnexal mass separate from the ovaries was diagnostic of ectopic pregnancy with a sensitivity of 81%, a specificity of 84 %, a positive predictive value of 71% and a negative predictive value of 90%. When a nonspecific adnexal mass can be found, care should be taken not to confuse it with corpus luteum cyst.

Free fluid in the cul-de-sac is

generally a nonspecific finding. In our series, it was identified in about 60% of cases and, when present, was a helpful adjunct to diagnosis. It was also identified in about one half of complete abortions and one third of corpus luteum cysts. It does not necessarily represent blood but may be caused by exudative secretion. Diffuse echoes within the sonolucent area are indicative of blood with clot and debris.

In this paper, fluid in the cul-de-sac was associated with a nonspecific adnexal mass in 19 patients but it was associated with an adnexal ring in only 3 cases. The presence of adnexal ring, nonspecific adnexal mass and free fluid in the cul-de-sac have a positive predictive value of 78.57 %, 71.43 % and 62.86 % respectively. The combination of a nonspecific adnexal mass and free fluid in the cul-de-sac increased the positive predictive value to 78.26%. On the other hand, the combination of an adnexal ring and free fluid in the cul-de-sac did not increase the positive predictive value. Adding a third ultrasound feature did not improve the test performance.

Other findings such as a nonspecific adnexal mass, an empty uterus, fluid in the cul-de-sac, and a decidual reaction in the uterus are all suggestive of an ectopic pregnancy but can be seen in other conditions. No patient in this study had coexistent intrauterine and extrauterine gestations. While a definite diagnosis of ectopic pregnancy is difficult to make, transvaginal sonography is often helpful in essentially excluding an ectopic pregnancy by

identifying an intrauterine gestational sac. This was the case in slightly more than 12% of our patients. The presence of a normal intrauterine gestation practically rules out the possibility of ectopic pregnancy. However, care must be taken that blood and hyperplastic endometrium within the uterine cavity (pseudosac), occasionally seen in patients with ectopic pregnancy, is not misdiagnosed as an intrauterine pregnancy. In these cases, the echogenic rim surrounding a normal intrauterine gestational sac and double sac sign can not be identified. Therefore, transvaginal ultrasound allowed earlier demonstration of an intrauterine pregnancy without confusion with a pseudosac.

The main limitation is the risk of obtaining a false positive diagnosis due to misinterpretation of the variants of the corpus luteum and complete abortion. A false negative diagnosis may be made in the case of an ectopic gestation that is located outside the true pelvis or in the event of very small tubal gestation. Ectopic nidation, especially within the abdominal cavity, between the leaves of the mesentery, or on the liver or spleen, makes sonographic visualization extremely difficult.

We mention the various transvaginal sonographic features that may cause differential diagnostic problems for the ultrasonographers. Three structures should be carefully examined and correctly recognized:

1. The corpus luteum, which is eccentrically located within the ovary, surrounded by ovarian tissue, may cre-

ate the impression of a "tubal ring".

2. Tubal pathologic conditions, such as a tubo-ovarian complex, which contains a heterogeneous hyperechoic content (nonspecific adnexal mass).

3. The endometriotic cyst.

A correct diagnosis of ectopic pregnancy can be made in approximately 80% of cases by the use of transvaginal sonography as the sole investigation. The number of false positive diagnoses continue to be high. Our study of ectopic pregnancy has shown less diagnostic accuracy of ultrasonography than those previously published<sup>(6)</sup>. Although the criteria described here may improve the value of an ultrasound examination for excluding ectopic pregnancy when there is clinical suspicion, the sole use of a transvaginal sonography will not reliably diagnose this life-threatening condition. It is suggested that the accuracy of sonography can be increased by determining the serum hCG level on the day of the scan and by interpreting the findings with reference to the discriminatory hCG zone. The combination of transvaginal sonography with serum  $\beta$ -hCG can reduce the false-positive rate<sup>(7)</sup>.

Transvaginal sonographically aided therapy of ectopic pregnancy was recently suggested by various authors. In our series, one case of tubal pregnancy was treated with Actinomycin D. In this method, the antimetabolic potential of this agent is exploited to hamper the growth of the ectopic pregnancy. This procedure should be followed by serial determination of  $\beta$ -hCG levels<sup>(8)</sup>, by repeated

transvaginal sonograms and by clinical evaluation. Bleeding or rupture of the ectopic pregnancy may occur following this procedure, therefore, careful observation is needed.

The result of this study supports the practice of using transvaginal sonography in the evaluation of patients with suspected ectopic pregnancies. Transvaginal sonography is a valuable diagnostic procedure as a complement to clinical data in evaluating patients with suspected ectopic pregnancy<sup>(6,9,10)</sup> and can be carried out at the time of pelvic examination when the clinical indication is first encountered. Our data indicate that certain sonographic features such as an adnexal ring or non-specific adnexal mass with intraperitoneal fluid are helpful in making the diagnosis of an ectopic pregnancy. However, transvaginal ultrasound, performed in conjunction with quantitative  $\beta$ -hCG assays, has increased the diagnostic accuracy, provided earlier diagnosis of ectopic pregnancy and contributed to reduction of maternal morbidity and mortality.

Because high frequency transvaginal sonography enables recognition of this disease at its early stages, clinicians should rely on this method with higher confidence compared to its transabdominal sonography. The transvaginal sonography, now widely available, is undoubtedly changing the scene in gynaecological practice in general and in the work up of the ectopic pregnancy in particular. Based on our few years experience, transvaginal sonography can be incorporated into

the routine diagnostic work up of patients suspected of having an ectopic pregnancy at Chulalongkorn Hospital. There is no need for special patient preparation. In about one-third of patients, suspected ectopic pregnancies were ectopic pregnancies. Today, in our department, transvaginal sonography has become a first line diagnostic test for any patient who is suspected of having an ectopic pregnancy, with the exception of extremely ill patients with acute shock.

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# Prenatal Sonographic Diagnosis of Ventral Abdominal Wall Defects : Case Series Report

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**Abstract :** *Fetal ventral abdominal wall defects require prenatal diagnosis for proper management. To evaluate the role of prenatal sonography in identifying characteristics of each type of defect, 12 cases were prospectively collected and followed. They consisted of 3 body stalk anomaly, 4 gastroschisis and 5 omphalocele. All of them were sonographically diagnosed with no false positive. All body stalk anomalies were uniformly fatal, 3 of the 4 gastroschisis and only 1 of the 5 omphalocele survived. All of the body stalk abnormal cases and 4 of the 5 omphalocele had other associated anomalies but there were none in the cases of gastroschisis. Better prognosis for neonates with gastroschisis appears to reflect the lower frequency of associated congenital anomalies and severity of the defect. (Thai J Obstet Gynaecol 1992;4:119-124.)*

**Key words :** gastroschisis, omphalocele, body stalk anomaly

The three main types of ventral abdominal wall defects detected by prenatal sonography are omphalocele, gastroschisis and body stalk anomaly<sup>(1-6)</sup>. They are associated with external herniation of abdominal contents but in omphalocele the defects are in the midline at the site of the umbilicus, whereas, gastroschisis is a paraumbilical defect usually located to the right of the midline. Body stalk anomaly is a severe abdominal wall defect due to failure of formation of the body stalk and is characterized by absence of the umbilicus and umbilical cord and the sac is covered by amnion and placenta. It is important to diagnose these two conditions in utero

in order to plan further management and detect other associated anomalies. Gastroschisis is essentially an isolated entity, whereas, omphaloceles are at risk for other abnormalities that include cardiac anomalies (ventricular and atrial septal defects, tetralogy of Fallot) up to 47 %, neural tube defects up to 39 %, gastrointestinal anomalies, and trisomies to 35 - 58 %<sup>(1)</sup>. Prenatal diagnosis of an omphalocele should prompt a careful search for additional anomalies as well as amniocentesis for chromosome study.

The objective of this case series is to study the characteristics of ventral wall defects in ultrasound findings and neonates.

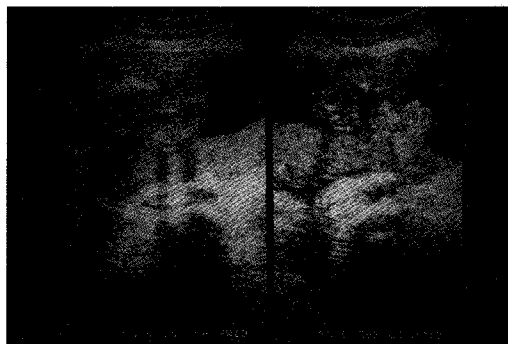
## Materials and Methods

Ultrasonographic prenatal diagnoses were performed by the authors, who were perinatal sonographers, from June 1989 to July 1991, using convex real-time scanner with a 3.5 MHz transducers (Aloka Model 650). Various indications required examinations including abnormal fundal growth, decrease of fetal movement, suspicion of twins, threatened abortion, etc.. The most important sonographic finding to differentiate between gastroschisis and omphalocele is the presence of the covering of membranes or not, eviscerated mass with covering membrane is omphalocele and without in the other. Body stalk anomaly is diagnosed when the fetus is attached to the placenta and large ventral defects allow protrusion of the viscera and the umbilical cord cannot be demonstrated<sup>(1)</sup>.

When the ventral abdominal wall defect is diagnosed, the obstetric and previous history were carefully reviewed and the patient followed until delivery.

## Results

Twelve cases of ventral abdominal wall defect were diagnosed in utero and followed by the authors. Of the 12 cases, 3 were body stalk syndrome, 4 were gastroschisis and 5 were omphalocele. The outcome of the neonates confirmed the ultrasound diagnosis in all cases. Demographic



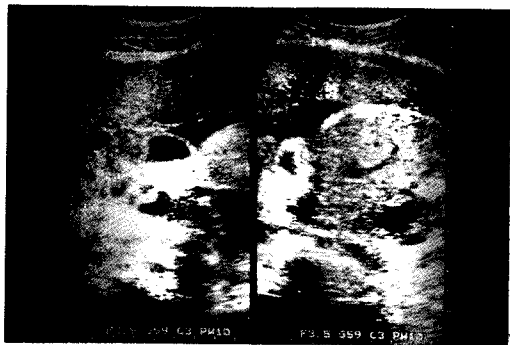
**Fig. 1** Sonogram of fetus with body stalk anomaly shows herniated viscera and in proximity with the placenta. The umbilical cord could not be identified (Case 2).



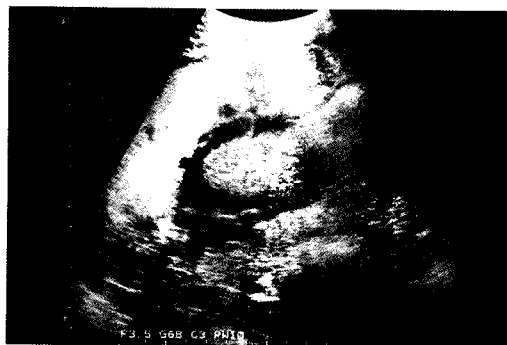
**Fig. 2** The figure shows severe ventral abdominal wall defect with large herniated viscera of body stalk anomaly. This fetus was absence of umbilical cord and had short limbs, kyphosis and scoliosis (Case 2).

information and ultrasound findings of these pregnancies are presented in Tables 1 and 2 respectively.

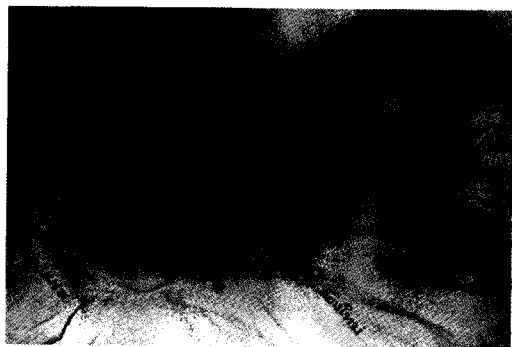
All of the body stalk anomaly were stillborns, 3 of the 4 gastroschisis and only 1 of the 5 omphalocele survived after surgical correction. All of body stalk anomaly and 4 of the 5 omphalocele had other associated anomalies but there were none in gastroschisis, however, no chromosome



**Fig. 3** The imaging illustrates floating bowel in the amniotic cavity of the fetus with gastroschisis (Case 6).



**Fig. 5** Omphalocele in a third trimester fetus. The herniated liver with peritoneal membrane coverings was seen (Case 10).



**Fig. 4** Newborn with gastroschisis. There is no covering membrane, and the defect is on the right paraumbilical area (Case 6).



**Fig. 6** Typical omphalocele of the newborn in the same case of Fig. 5.

**Table 1** Demographic data of the pregnancies

No.	Age (Years)	Parity	Weeks of diagnosis	Weeks of delivery	Maternal complications	Indications for ultrasound exam.
1.	35	2-0-0-1	19	20	Elderly gravida	Threatened abortion
2.	20	0-0-0-0	21	21	-	No fetal heart beat
3.	23	0-1-1-1	24	40	-	Decreased movement
4.	20	0-0-0-0	26	39	-	Decreased movement
5.	21	1-0-0-1	32	37	-	? IUGR
6.	42	1-0-3-1	34	38	Elderly gravida	? IUGR
7.	27	2-0-0-2	36	40	Gestational DM	Gestational DM
8.	30	2-1-0-2	29	35	Premature labour	? IUGR
9.	29	1-0-1-1	20	21	-	Small for dates
10.	25	0-0-0-0	35	36	Premature labour	Decreased movement
11.	22	0-0-1-0	28	29	Twins	Large for dates
12.	21	0-0-1-0	24	40	-	Uncertain dates

**Table 2** Ultrasound findings and neonatal outcomes

No.	Ultrasound findings and diagnosis	Mode of delivery	Neonatal outcomes
1.	Body stalk anomaly, absence of umbilical cord, deformity of chest wall, short limbs, normal amniotic fluid, herniated viscera & membrane coverings.	Therapeutic abortion with Sulprostone	Male, stillbirth, body stalk anomaly, absence of umbilical cord, deformity of chest wall, short limbs.
2.	Body stalk anomaly, absence of umbilical cord, short limbs, kyphosis, scoliosis, no heart beat, decreased fluid, herniated viscera & membrane coverings.	Therapeutic abortion with Sulprostone	Male, stillbirth, body stalk anomaly, absence of umbilical cord, short limbs, kyphosis, scoliosis.
3.	Body stalk anomaly, anencephaly, absence of umbilical cord, large VSD, decreased fluid, herniated viscera & membrane coverings.	Normal delivery	Female, stillbirth, large VSD, body stalk anomaly, large eviscerated mass, anencephaly.
4.	Gastroschisis, herniated bowel & coverings at Rt paraumbilicus, oligohydramnios.	C/S	Male, Apgar scores 9,10, gastroschisis, surgical correction, survived.
5.	Gastroschisis, herniated bowel & covering at Rt paraumbilicus, normal fluid, low lying placenta.	C/S	Female, Apgar scores 7,9, gastroschisis, IUGR, surgical correction, dead from sepsis.
6.	Gastroschisis, herniated bowel & covering at Rt paraumbilicus, normal fluid, normal growth.	C/S	Male, Apgar scores 8,10, gastroschisis, surgical correction, survived.
7.	Gastroschisis, herniated bowel & coverings at Rt paraumbilicus, normal fluid, normal growth.	C/S	Female, Apgar score 10,10, gastroschisis (only small bowels), surgical correction, survived.
8.	Omphalocele (liver & bowel & membrane coverings), ? IUGR, oligohydramnios.	Normal delivery (advanced labour on admission)	Male, Apgar scores 8,10 omphalocele, IUGR, surgical correction, survived, normal chromosome, no other anomaly.
9.	Large omphalocele, (mass & membrane coverings) very short femurs, deformity of spines, normal amniotic fluid, small head circumference, mild fetal ascites.	Normal delivery	Male, stillbirth, IUGR, normal chromosome, large omphalocele (liver & bowel), very short femurs, deformity of spines and pelvis, microcephaly.
10.	Large omphalocele (liver & bowel & membrane coverings), oligohydramnios, no IUGR, mild fetal ascites.	C/S	Male, Apgar scores 8,9, large omphalocele, bowels necrosis, VSD, surgical correction dead from sepsis, normal chromosome study.
11.	Conjoined twins (Thoracopagus), one heart, meningocele and omphalocele of one fetus (liver & bowel & membrane coverings), normal fluid.	C/S	Both female, stillbirth, gastroschisis of both liver and bowels and sacral meningocele in one fetus, conjoined twins (Thoracopagus), one heart.
12.	Omphalocele (liver & bowel & membrane coverings), anencephaly, normal fluid.	Normal delivery	Female, stillbirth, anencephaly, large omphalocele.

C/S = Caesarean section

disorder was detected in all cases of this study. Additionally, 3 of the 9 omphalocele and gastroschisis had birth weights below the 10th percentile.

## Discussion

In omphalocele, the umbilical cord inserts into the membrane surrounding the herniated mass, whereas

in gastroschisis the cord inserts normally into the fetal abdomen. A membrane consisting of amnion and peritoneum surrounds the herniated contents of an omphalocele but gastroschisis represents a full thickness abdominal wall defect without the covering membranes, so the herniated bowel loops float freely in the amniotic fluid<sup>(1-4)</sup>. Unprotected by a membrane, and at risk for ischemic events and necrosis as in one case in this report, the eviscerated bowel is prone to secondary complications, including thickening and fibrosis. Interestingly, all cases with sonographic demonstration of eviscerated liver were omphalocele, but only the small bowel is eviscerated in all cases of gastroschisis. This finding supports the previous report which found that only the small bowel is eviscerated in most cases of gastroschisis<sup>(2)</sup>. Therefore, sonographic demonstration that the liver has herniated through an abdominal wall defect is considered strong evidence for omphalocele.

This report suggests that ventral abdominal wall defects increase the incidence of oligohydramnios (3 in 10) which may represent other anomalies or fetal distress. Oligohydramnios may lead to poor quality of ultrasonic imaging and make it difficult to differentiate between gastroschisis and omphalocele.

We found fetal ascites in only two cases of omphalocele, but not in gastroschisis, this may be explained by the absence of a covering membrane in gastroschisis allowing ascites to

escape into the surrounding amniotic fluid.

In conclusion, in spite of this small series, it was shown that omphalocele is associated with other anomalies more often than gastroschisis. Some sonographic characteristics other than the presence of membrane covering, i.e. fetal ascites, liver in herniated mass, other anomalies, may help in the distinction between these two conditions. For body stalk anomaly, it is always lethal. Sonography can be used to accurately diagnose ventral wall defects in utero and can distinguish between body stalk anomaly, gastroschisis and omphalocele in most cases.

### Acknowledgement

The authors would like to thank the Ultrasound Unit staffs of Radiology Department for their kind cooperation and valuable help. We are most grateful to Associate Professor Kamjad Swadio and Associate Professor Suri Simarak for their encouragement.

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# Urinary Drainage Following Radical Hysterectomy

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**Abstract :** *From July 1987 to December 1989, 66 patients with early stage cervical and endometrial cancers underwent radical hysterectomy and pelvic nodes dissection at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University. To compare the rate of lower urinary tract complications after surgery, the patients were voluntarily placed on transurethral or suprapubic catheterization. Postoperative morbidities were observed. The only advantage of suprapubic catheterization observed was the absence of urinary incontinence (0/27), while 15% (6/39) were observed in another group ( $p=0.03$ ). All other studied parameters were the same in both groups. (Thai J Obstet Gynaecol 1993;4:125-128.)*

**Key words :** radical hysterectomy, complications, drainage

Radical hysterectomy and pelvic nodes dissection is the treatment of choice for stage IB and IIA cervical and endometrial cancers, which comprises about 15% of the cases. More than 50 cases a year are operated on in this hospital nowadays. The surgical procedure itself places the bladder at considerable risk of complications including injury, dysfunction and infectious morbidity. At the institute, although intraoperative injury to the urinary tract is rare, urinary dysfunction with urinary tract infection continue to be the most significant complications following radical hysterectomy. The incidence of

the complications ranges from 16 to 87% in most reports<sup>(1,2)</sup> and a variety of surgical techniques, inconsistent radiation therapy and differences in perioperative management of bladder drainage render a comparison of published data infeasible. Uniform estimation of long-term results is almost impossible owing to changes in surgical techniques and perioperative regimens. A recent review of radical hysterectomy at Srinagarind Hospital revealed 61.5% of bladder dysfunction and 21.5% of urinary incontinence<sup>(3)</sup>. Suprapubic bladder drainage was reported to be more valuable in reducing lower urinary tract

complications<sup>(4)</sup>.

This study was carried out to compare the rate of lower urinary tract complications in both suprapubic and transurethral catheterization groups.

### Materials and Methods

#### Patients

The patients enrolled in this study were those who had histologically proven cervical cancer stage IB to IIA or endometrial cancer stage II who had

undergone radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, from July 1987 to December 1989. The surgeons were the staffs of the Division of Gynaecologic Oncology, Department of Obstetrics and Gynaecology. The operative techniques performed in this hospital were class III extended hysterectomy as Piver's classification<sup>(5)</sup> and the modified Okabayashi technique as mentioned by Sekiba<sup>(6)</sup>. Those who had contraindication for radical surgery were

**Table 1** Patients' characteristics

Characteristics	TUC n=39	SPC n=27
1. Mean age	45.23±9.17	40.29±10.20
2. Mean weight	56.44	52.44
3. Stages :		
IB	36	24
IIA	3	1
IIB	0	2
4. Prior conization	3	0*
5. Prior radiation	1	1
6. Prior chemotherapy	1	2
7. Techniques :		
Wertheim-Meig	21	5
Okabayashi	18	22*
10. Surgeons		
1	13	13
2	19	3
3	5	9
4	2	2
11. Mean operation time (min)	193.08±33.08	201.67
12. Mean blood loss (ml)	1297.05±659.43	1266.67±1016.02
13. Mean blood transfusion (units)	2.97±1.55	2.74±2.09

\* Statistical significant

TUC= Transurethral catheterization

SPC= Suprapubic catheterization

excluded from the study. The patient's characteristics are shown in Table 1.

### Method

The patients were voluntarily selected into 2 groups: group 1 were placed on transurethral catheter and group 2 were placed on suprapubic catheter at the end of surgery. The patients were observed for postoperative urinary functions clinically from the 7th postoperative day until they were discharged from the hospital and then three monthly in the first year and six monthly after that. Bladder dysfunction was defined as an inability of the bladder to contract and initiating urination from both hypertonic and atonic phase. Urinary incontinence was defined as the observation of involuntary loss of urine at normal circumstances or increase intraabdominal pressure. Difficulty in urination was defined as the difficulty or inability to urinate due to mechanical urethral defect and not from the bladder cause. Residual urine was the volume of fluid remaining in the bladder immediately following micturition.

### Results

With the minimum time of follow-up of at least 11 years of observation of postoperative morbidities, the urinary complications of both groups of patients are shown in Table 2. There was no urinary incontinence in the suprapubic group while 6 patients (15.4%) of the transurethral group were observed. Table 3 shows the infectious

morbidities of the two groups and all parameters were the same.

### Discussion

The aetiologies of disorders of the lower urinary tract after radical pelvic surgery range from lesions of the

**Table 2** Postoperative morbidity

Morbidity	TUC N=39	SPC N=27
1. Bladder dysfunction	31	18
2. Urinary incontinence	6	0*
3. Difficulty urination	5	4
4. Residual urine day	10.84	24.44
5. Postop. hospitalization	17.71	17.48

\* Statistical significant

**Table 3** Infectious morbidity

Morbidity	TUC N=39	SPC N=27
1. Febrile morbidity	18	15
2. Generalized sepsis	3	2
3. Urinary tract infection	24	16
4. Other non-surgical site infection	23	17

pelvic nerves and postural changes of the bladder in an empty pelvic cavity to involuntary lesions resulting from insufficient perioperative bladder drainage and urinary tract infections. The majority of the nerves from the pelvic plexus which supply the bladder pass over and

around the vagina. Any operation involving excision of the paracervical and paravaginal web of retroperitoneal tissue will interrupt some portion of bladder innervation. Some of the fibers pass around the lateral aspects of the vagina, deep dissection tends to include the paravaginal portion of the web, however, complete interruption of innervation is rare. As the only site of parasympathetic to the bladder entry, the more the operation goes lateral and deeper into the parametria, the greater the complications of the urinary tract. Complications from radical hysterectomy and pelvic nodes dissection are still inevitable sequelae. It is increased when surgery is followed by radiotherapy in those high risk patients. Bladder dysfunction is the most common complication and attempts have been made to overcome the problem. Prolonged bladder drainage has been recommended to prevent over distension in the early hypertonic phase. van Nagel et al<sup>(4)</sup> recommended suprapubic cystostomy to be superior to urethral catheter. Kadar and Nelson<sup>(7)</sup> recommended voiding by the clock in combination with Crede's maneuver or intermittent self catheterization is more acceptable.

From our limited clinical experience and without urodynamic study, suprapubic catheterization has

benefit in prevention of urinary tract complications. Attempts must be focussed on the more practical and acceptable way for the patients, nurses and other health personnel who take care of those postoperative patients.

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# Menopausal Symptomatology and Hormonal Correlation

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**Abstract :** *To assess the correlation between climacteric symptoms and objective measurement of hormonal changes in women suffering from natural and surgical menopause, we conducted measurement of serum concentration of follicle stimulating hormone (FSH), luteinizing hormone (LH), and estradiol ( $E_2$ ) by radioimmunoassay on 48 Thai women attending the menopausal clinic at the Department of Obstetrics and Gynaecology, Chulalongkorn Hospital. When comparing the hormonal levels with modified estrogen-deficiency-symptom scoring system, using correlation and regression analysis, the results showed that there was no statistical correlation between hormonal levels (neither FSH, LH nor  $E_2$ ) with total symptomatological scores. However, when comparing each hormonal profile with detailed a symptom scoring system, the analysis revealed that there was positive correlation between FSH and sexual symptom scores such as less sex drive, less sex feeling, dry vagina and dyspareunia ( $r = 0.392$ ). (Thai J obstet Gynaecol 1993;4:129-133.)*

**Key words :** menopause, symptomatology, hormonal correlation

Women are the largest consumers of the health care system. As our population ages, more women are in their postmenopausal years. Entering this period, some women develop the so-called "Climacteric Syndromes" that seem to be a less serious phenomenon in Asian people than in other parts of the world.<sup>(1)</sup> However, climacteric syndromes have always been subjective symptoms, only a few studies have evaluated this syndrome in an objective way. On the other

hand, there are a lot of climacteric-like symptoms that can be found in women not entering the menopausal period. To assess the correlation between climacteric symptoms and objective measurement of hormonal changes in women suffering from this syndrome, we measured the serum follicle stimulating hormone (FSH), luteinizing hormone(LH) and estradiol ( $E_2$ ) on patients attending our menopausal clinic.

## Materials and Methods

The study included 48 women who attended the menopausal clinic, Department of Obstetrics and Gynaecology, Chulalongkorn University Hospital, Bangkok, Thailand, from March to July, 1992 mainly because of vasomotor symptoms, such as hot flushes and sweats. Their mean age was 49.3 (SD=4.0, ranged 40-59) years with amenorrhoeic duration of more than 12 months in 18 cases, more than 6 months in 20 cases, less than 6 months in 17 cases, unknown menstrual history in one case and 10 cases still having menstruation. These women were not on other hormonal replacement therapy, did not have any endocrine disorders nor receiving any steroid hormonal treatment. They had no chronic illnesses such as diabetes mellitus, chronic renal diseases or received regular medication or investigations with radioisotope/radiocontrast medium within one week. All of the women had spontaneous cessation of menses, except three, who had surgical menopause. None of the women smoked or drank. An interview was undertaken on all the women, including demographic data, menstrual history, medical history and especially perimenopausal/postmenopausal complaints using modified estrogen-deficiency scoring system (Table 1)<sup>(2)</sup>. In addition, physical and pelvic examinations were performed and 20 ml of blood was obtained for the determinations of FSH, LH and estradiol radioimmunoassay. Then, the hormo-

nal levels and modified estrogen-deficiency scoring system were compared, using correlation and regression analysis and  $\chi^2$ -test.

**Table 1** Modified estrogen-deficiency-symptom scoring system<sup>(2)</sup>

Symptoms	Date/Score	Date/Score
1 Hot flushes		
2 Headaches		
3 Irritability		
4 Depression		
5 Unloved feelings		
6 Anxious feelings		
7 Anxious sleeplessness		
8 Unusual tiredness		
9 Bachache		
10 Joint pains		
11 Muscle pains		
12 New facial hair		
13 Unusual dry skin		
14 Less sex drive		
15 Less sexual feelings		
16 Dry vagina		
17 Dyspareunia		
18 Dysuria		
19 Frequency		
20 Incontinence		
Total score		

0 = Absence, 1 = Mild, 2 = Moderate,  
3 = Severe

## Results

When comparing FSH, LH, E<sub>2</sub> and each classified action of the modified estrogen-deficiency scoring system, the results are presented in Table 2.

**Table 2** Correlation analysis

Correlation	Age	E <sub>2</sub>	FSH	LH
E <sub>2</sub>	-.3451 *			
FSH	.3822 *	-.3682 *		
LH	.3830 *	-.2267	.8387 **	
ACT 1-8	-.2237	.1214	-.2331	-.2323
ACT 9-11	-.0161	.0814	-.0872	-.0172
ACT 12-13	.1076	.0295	.1837	.2769
ACT 14-17	.0632	-.1363	.3972 *	.1215
ACT 18-20	.0689	.1757	.0978	-.0062
TOTAL SCORES (ACT 1-20)	-.1386	.0938	-.1235	-.1604

\* p = .01, \*\* p = .001

From the correlation analysis, it shows that age has a statistically significant negative correlation with serum E<sub>2</sub> and positive correlation with FSH and LH. Estradiol has statistically significant negative correlation with FSH, and FSH has statistically significant positive correlation with LH and actions 14-17.

### Discussion

This study demonstrates that with increasing age, estradiol has a tendency to decline. On the other hand, FSH and LH have a tendency to increase which may be explained by E<sub>2</sub> from a group of 10 women who are still menstruating and have climacteric symptoms. This is because after 35 years of age, the human ovary begins to decrease in weight and size and contains fewer oocytes, follicular structures and has more atretic and degenerating follicles. This loss of

oocytes and follicles ultimately results in a gradual diminution of estrogen and inhibin<sup>(3)</sup>, which causes the reduction of estradiol and increment of FSH level.

Considering the correlation among E<sub>2</sub>, FSH and LH, the results showed that estradiol had statistically significant negative correlation only with FSH (Fig. 1), and FSH had positively a very close correlation with LH (Fig. 2). From the results above, we suggest that, women who are suspected of entering the climacteric symptoms and require hormonal investigations to establish the diagnosis, may be checked only for E<sub>2</sub> and FSH level to lessen the high cost of hormonal assay for LH due to its close correlation to FSH.

When comparing the hormonal levels (FSH, LH and E<sub>2</sub>) with modified estrogen-deficiency scoring system, it showed that there was no statistical correlation between the hor-

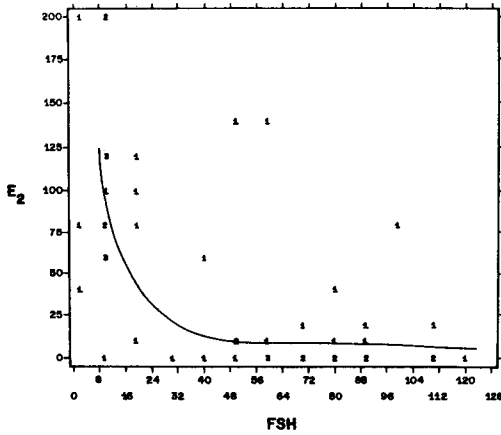


Fig. 1 Correlation between  $E_2$  and FSH

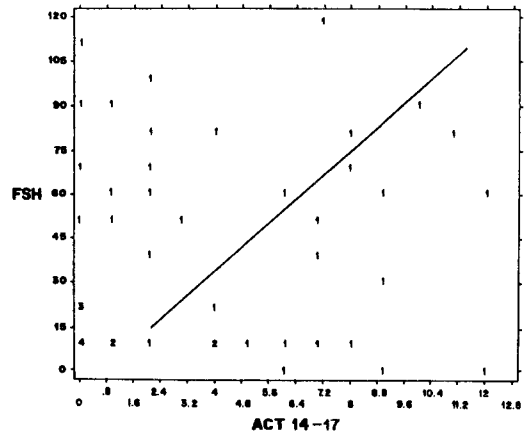


Fig. 3 Correlation between LH and FSH

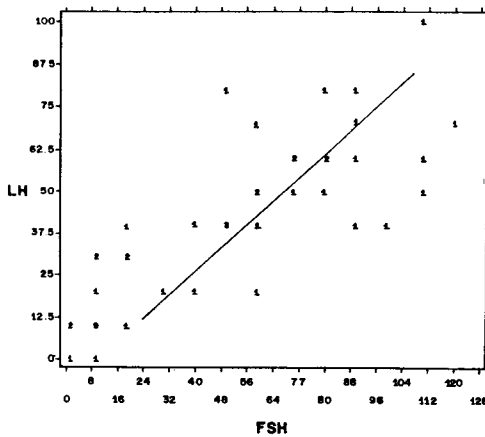


Fig. 2 Correlation between FSH and sexual feeling

monal levels and total symptomatological scores. This may be extrapolated that one cannot use the presence or absence of climacteric symptoms to indicate the need or no need for hormonal replacement therapy (HRT). For example, women with low symptomatological scores might have significant hormonal change that requires HRT to prevent bone loss. However, when considering each ac-

tion scoring system as classified above, we found that FSH has statistically significant correlation with actions 14-17 (Fig. 3) which were sexual symptoms, such as less sex drive, less sex feelings, dry vagina and dyspareunia. This may be explained by the fact that the recruited subjects were women suffering from vasomotor symptoms in the age group of 40-59 years, 10 of 48 cases still menstruate and 17 of 48 cases had amenorrhoeic duration of less than six months, plus the fact that the decreasing inhibin occurred several years before the menopause, resulting in an elevation of FSH, the first laboratory indication of the perimenopause.<sup>(4)</sup> Thus, it may be these menstruating subjects who made the result show significant correlation between FSH and actions 14-17 without significant correlation between  $E_2$  and actions 14-17, though it is theoretically accepted that estrogen deficiency results in epithelial and connective tissue atrophy at the vagi-

nal wall, causing vaginal dryness and dyspareunia<sup>(5)</sup>. From the low correlation between hormonal level and the symptom scoring system in this study, it may be explained that menopausal symptomatology may not solely depend on hormonal changes, familial, social and environmental factors should also be considered when dealing with these groups of clients. Nevertheless, further study on these issues are continuing with increasing subjects and the final results will be presented in the near future.

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# A Possible New Approach to the Postmenopausal Osteoporosis Treatment with Calcitonin Originating from the Human Fetal, Neonatal and Juvenile Calf Thymus

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**Abstract :** *Thymus is, according to the contemporary opinion, a part of the hypothalamus-pituitary-thymus-gonadal axis and participates in the regulation and modulation of the endocrine reproductive function in humans. We studied the endocrine properties of the thymic gland and found that it contained significant calcitonin activity in the specimens of the human fetal and neonatal thymus as well as in the juvenile calf thymus. We stress on the interesting fact that calcitonin presence in the human fetal and neonatal thymus is in correlation with calcitonin levels in human neonatal umbilical cord. Application of thymic extracts with calcitonin activity presents the possibility of a new therapeutical approach to osteoporosis. (Thai J Obstet Gynaecol 1993;4:135-138.)*

**Key words :** calcitonin, thymus, postmenopausal osteoporosis

Calcitonin is a polypeptide hormone which in mammals is produced by parafollicular C cells of the thyroid gland. It contains 32 AA, molecular weight approximately 3500 D<sup>(1)</sup>. Its role in the development, prevention, and treatment of osteoporosis has been highlighted during the past few years. Calcitonin presents a strong hypocalcemic effect and the property to inhibit osteoclasts activity, thus

preventing bone resorption, which is of the special importance in the postmenopausal period<sup>(2-6)</sup>. So, calcitonin administration inhibits bone resorption by a direct action on the activity of the osteoclasts. Long-term treatment with calcitonin seems not only to inhibit osteoclasts activity, but also to decrease their number. Investigations of endocrinological properties of the human fetal (FTH) and neonatal

thymus (NTH) confirmed the production of calcitonin<sup>(7-9)</sup>.

According to the contemporary opinion, thymus is part of the hypothalamus-pituitary-thymus-gonadal axis and participates in the regulation and modulation of the endocrine reproductive function in humans<sup>(10,11)</sup>. We studied the endocrine properties of the thymic gland and found that it contained significant calcitonin activity in the specimens of the human fetal, neonatal, as well as in the juvenile calf thymus (JCTH).

In the thymus gland many different hormones have been localized, including oxytocin, vasopressin, beta-endorphins, etc.<sup>(11-13)</sup>. Contemporary investigations of the thymic vascular pattern confirmed that this gland can be of special importance in the production of a great variety of other hormones<sup>(14)</sup>. The aim of this study was to confirm calcitonin production in the human fetal and neonatal thymus as well as in the juvenile calf thymus gland.

### Materials and Methods

This study was performed in collaboration with the Department of Clinical Pathology of Gynaecology and Obstetrics Clinic, University Clinical Center in Belgrade, Institute for Thymus Research, Bad Harzburg, Germany and Institute of Anatomy, School of Medicine, Belgrade, Yugoslavia. We determined the concentrations of calcitonin in human fetal (n=3) and neonatal (n=3) thymus au-

topsy specimens obtained immediately after spontaneous preterm labour and delivery by using the method of quantitative bioassay on experimental animals (rats, n=20) after administration of FTH, NTH and JCTH. Concentrations of calcitonin were estimated by the method of photometry on LP 400/s (Lange test). Obtained data were expressed (mean) in IU/mg of thymus wet tissue weight that were also calculated in ng/l. Calcitonin concentrations were also determined in human neonatal cord blood specimens (n=20).

### Results

Calcitonin bioactivity was found in FTH (0.40 IU/mg wtw or 93.60 ng/l) and NTH (0.43 mg wtw or 100.62 ng/l). These findings were expressed in JCTH (0.39 IU wtw or 91.26 ng/l) showing also significant activity in the animal thymus gland (Fig. 1).

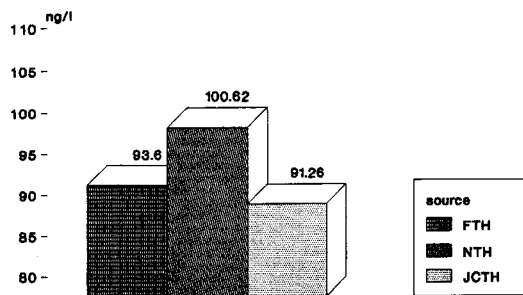


Fig. 1 Calcitonin activity in thymus.

We stress on the interesting fact that calcitonin presence in the

FTH, NTH and JCTH is in correlation with calcitonin levels in umbilical human neonatal cord (87.5 ng/l).

## Discussion

The presence of hormones in thymus and their endocrinological function has not been systematically investigated until now. The immune and endocrine system appear to be able to communicate with each other by the signal hormonal molecules and receptors common to both systems<sup>(12)</sup>. Thus, the thymic extract administration in experimental animal conditions unevenly increases calcium and phosphorus levels in all the bones most notably in the long bones and demonstrates the positive influence of thymus in ossification processes. It is of possible interest, the relationship between thymic and parathyroid gland as well as the influence of thymic peptides on PTH levels.

Thymic calcitonin production was confirmed 25 years ago by Galante and Gudmundson<sup>(15)</sup>. In the following years, calcitonin receptors were discovered in cellular substrates of CNS, hypophysis, and the lymphoid system, etc.. The obtained results in this study could suggest that the identified calcitonin production in the endocrine zone of thymus gland represent the important factor in the regulation of calcium bone metabolism in the fetal and neonatal period as well as in the other life periods. Whilst oestrogen is the preferred treatment in postmenopausal patients,

calcitonin as an antiresorptive drug has been experimentally shown to be of use in women who do not wish to experience withdrawal bleeding. Application of thymic extracts with calcitonin activity presents the possibility of a new therapeutical approach to postmenopausal osteoporosis. Women who have established osteoporosis can be offered a number of treatments which appear to be effective in preventing further bone loss and restoring bone formation.

Endocrinology of the thymus gland requires further investigation in order to obtain a definitive exact insight in human reproduction especially in the processes of protection against osteoporosis in the postmenopausal period.

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