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Development of an In Vitro Fertilization and Embryo Transfer Programme : Preliminary Experience

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Abstract : *From October 1986 to August 1988, a total of 256 cases of infertile women with ages ranging from 26 to 42 years were admitted for the IVF & ET programme. Bilateral tubal occlusion and pelvic endometriosis were the most common indications. A combination of clomiphene citrate and hMG (211 cases) or hMG alone (45 cases) were used for superovulation. The average estradiol levels on the day of hCG administration was 1738 ± 761 pg/ml. Oocytes were retrieved by either laparoscopy (78 cases) or vaginal ultrasound guidance (178 cases). One hundred and five cases were cancelled (41%) due to poor response and premature LH surge. A total of 542 oocytes were collected and 312 oocytes were fertilized giving a fertilized rate of 57.5%. Embryos at 2 or 4 cells stage were transfered in 151 cases chemical and clinical pregnancies were diagnosed in 30 cases. (Thai J Obstet Gynaecol 1991;2:1-6.)*

Key words : in vitro fertilization, embryo transfer programme

The birth of the first test-tube baby on July 25, 1978 was considered a medical breakthrough of reproductive technology that involved superovulation, oocyte recovery, extracorporeal fertilization and replacement of fertilized egg[1]. This milestone was the culmination of many years of studies in animals that involved various rodents and the mammalian system[2]. The techniques of human in vitro fertilization embryo replacement have generated tremendous interest in both biologists and clinicians. The techniques are constantly changing and improving but important clinical information is now being obtained that offers many new approaches to the study and treatment of various aspects of tubal infertility that were not possible in the past[3-6]. In this report, we describe the development and experience of the in vitro fertilization and embryo transfer programme at Human

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Development

An extensive experiment of culturing 2-cell stage of mouse embryo (Balb-C/CD-1) began in mid 1985. Two-cell stage of mouse embryos which were fertilized in vivo, were further cultured in vitro and allowed to grow up to blastocyst. After achieving development to blastocyst in more than 70%, it was then decided to start on human oocytes fertilize in vitro[7]. The successful in vitro fertilization of a human oocyte in our laboratory was done on March 26, 1986. The first attempt of transferring 4-cell stage human embryo was done on June 12, 1986 but failed to concieve. The first birth from our IVF & ET programme in Thailand was a healthy male infant on August 15, 1987[7].

Patients and treatment protocol

From October 1986 to August 1989 a total of 256 infertile women with ages ranging from 26 to 42 years were admitted to the IVF & ET programme. The couples had a duration of infertility of 2 years or more (mean 8.4 ± 3.2 SD: range 2-17 years). All patients had previously undergone investigation for their infertility problems including semen analysis, laparoscopy, hysterosalpingography and hormonal assessment. Infertile couples attending our clinic can be classified into four categories 1) pure tubal factors, 2) pelvic endometriosis with previous surgery, 3) male factors, and 4) mixed infertility.

The majority of cases (211 patients) were treated with clomiphene citrate (CC) (Clomid, Merrel Dow, USA) 100 mg in divided doses from days 3 to 7 of the menstrual cycle and 150-225 IU of human menopausal gonadotropin (hMG) (Pergonal, Serono, Switzerland or Humegon, Organon, Holland) given intramuscularly, started on day 7 until follicular maturation was reached. Forty-five patients were superovulated with 2-3 ampules (150-225 IU) of hMG per day starting on days 3 of the menstrual cycle onwards until hCG was administered. With both treatments serum estradiol (E2) and follicular development were being monitored daily from day 6 onwards. A constant rise of E2 over 5-6 days coupled with at least 2 leading follicular diameter of 17-18 mm or more, 10000 units of human chorionic gonadotropin (hCG, Profasi, Serono, Switzerland or Pregnyl, Organon, Holland) were administered intramuscularly at 08:30 pm. 34-36 hours after hCG was given, oocytes were retrieved by either laparoscopy (78 cases) or ultrasonically guided transvaginal puncture (178 cases). The average estradiol levels on the day of hCG administration of CC/hCG treatment were 1738 ± 761 pg/ml (range 316 - 3691 pg/ml). Each mature follicle was aspirated with single lumen needle (Swemed, Sweden) with constant pressure (100-120 mmHg). Aspirating fol-

licles were flushed with Ham's F-10 medium. The oocytes were immediately washed and classified as previously described[8] and then transferred into a Falcon tube containing 1 ml of Ham's F-10 supplemented with 10% heat inactivated preovulatory patient's serum. The tubes containing oocytes were placed in an incubator under an atmosphere of 5% CO_2 in air for 4-6 hours prior to insemination.

The husband's semen was collected $1\frac{1}{2}$ hours after oocytes recovery. Liquified semen was washed twice in culture medium and the final sperm pellet was over-layered with 2-3 ml of fresh medium. After incubation for 15-30 min, the top 1 ml of the over lay was collected which contained the motile good quality sperm for insemination. Two incubated oocytes in the tube were inseminated with 0.1 x 10^6 ml spermatozoa and fertilization was confirmed at pronuclear check after 18-20 hours of insemination. The fertilized egg was then transferred into a 4-well dish containing fresh medium. Eggs that were not fertilized were re-inseminated. Follow up was done 24 hours after culture, the embryos at 2 to 4-cell stage (maximum of 4 embryos/patient) were transferred into the uterus using a Cook's catheter.

The patients were placed in dorsal lithotomy position with head tilted down. The external genitalia was cleaned with normal saline and prepped. The cervix was exposed with a bivalve speculum and the ectocervix was gently cleaned of cervical mucus with small swabs soaked with normal saline then swabbed with culture medium. The outer sleeve of the Cook's catheter was passed through the cervical canal and held at mark. The embryos were then loaded into the internal catheter with 30 µl of culture medium supplemented with 50% serum. The catheter was then passed through the outer catheter into the uterine cavity and fixed. The outer catheter was gently withdrawn for about 5 cm and both catheter were fixed at this position for one minute. The embryos were expelled by depressing the one ml syringe by 0.02-0.03 ml. The catheters were gently withdrawn and promptly checked microscopically to ensure the embryo had not been retained. Half an hour later the patient was transferred maintaining the position at the time of transfer and allowed home 4-6 hours later. The luteal phase was supported by administration of 1500 IU of hCG on day of transferring embryos and on day 4,7,10 and 13 after the embryo was transferred. Progesterone 50 mg (Schering AG, Germany) was injected intramusculary for 5 consecutive days starting on the day of oocyte recovery. Pregnancy was confirmed by assaying serum β-hCG 14 days after embryo transfer. At 7-8 weeks pregnancy was further confirmed by ultrasound. Amniocentesis in most of the cases was performed at 16-20 weeks of gestation.

Results

The age distribution of the IVF

patients (n=256) is given in Table 1. Of the 256 patients, 62% were more than 35 years. Only 9% of the patients who were in their twenties went through the IVF treatment programme. The analysis of the four main categories of referal were tubal occlusion/ adhesion (54.3%), pelvic endometriosis (31.3%), oligospermia (10.5%), and idiopathic (3.9%). Details of the patients treated for 256 cycles are given in Table 2. In all, 105 treatment cycles were cancelled at different stages due to poor response 38 cases (14.8%), failure to retrieve oocytes 10 cases (3.9%), failure to fertilize oocytes 21 cases (8.2%), or premature LH surge 36 cases (14%). It was possible to recover oocytes obtained for fertilization and trasfer of embryos for 151 treatment cycles. A total of 542 oocytes were collected and 312 fertilized giving a fertilization rate of 57.5%. An average of 2.0 embryos were transfered per patient. The pregnancy outcome and the type of pregnancy are given in Table 3. A total of 18 patients had β-hCG>20 mIU/ml 14 days after the embryo transfer. However, 6 pregnancies were lost due to abortion during the first trimester and ectopic pregnancy. Two healthy infants were born and 4 are on going pregnancies (>16 weeks).

Table 1 Age distribution of the IVF & ET patients (N=256)

Age (years)	No. of patients (%)
< 29	22 (9.0)
30-34	73 (28.9)
35-39	123 (46.9)
> 40	38 (15.1)

(Mean 35 ± 3.5, min = 26, max = 42)

Table 2 Details of treatment cycles (n=256)

Categories	No. of patients	(%)
Cancellation	105	(41)
Poor response	38	(14.8)
Failed to retrieve	10	(3.9)
Failed to fertilize	21	(8.2)
Premature LH surge	36	(14)
E2 peak (pg/ml)	1738 ± 761	
No. of oocytes collected	542	
No. of oocytes/puncture	2.8	
No. of oocytes fertilized	312	
Fertilization rate	57.5	
No. of embryo transfer/case	2.0	

Table 3 Success of 151 embryo transfer

Outcome	No. of cases
Chemical pregnancies (B-hCG>20 mIU/ml)	18
Clinical pregnancies	12
Abortion (2-3 m)	4
Ectopic	2
Term pregnancies	2
On going (>16 weeks)	4
Total	12

Discussion

A large proportion of the patients (62%) who went through our IVF & ET programme were older than 35 years and it is well documented that the IVF & ET prognosis for such patients is poor. A recent study demonstrated that the age of the patient was significantly affected by

their response to stimulation, and also the outcome of treatment[9]. Comparing women >35 years, 27% failed to reach oocyte recovery compared with 15% <35 years. Women over the age of 35 years had a reduced chance of implantation which supports previous findings[10].

As shown in the results, the stimulation protocol used for most of the patients was clomiphene citrate and hMG. Furthermore, the occurrence of premature LH surges in some patients making it difficult to time the oocyte collection which can result in the recovery of poor quality oocytes and failed fertilization. Premature luteinization and the spontaneous LH surge have been shown to reduce the successful outcome of IVF cycle[11,12]. In the past five years GnRH has been introduced to inhibit endogenous gonadotropin output and subsequently augment follicular growth with hMG[13].

In this paper, sperm problems were not mentioned. Some patients were cancelled due to failed fertilization mainly associated with poor quality sperm (oligoasthenospermia). Fertilization at an acceptable rate was maintained for the normospermic group. Estimates of defective sperm function or sub-normal seminal characteristics in nearly 35% of infertile couples suggests that this is the defined cause of human infertility[14]. In addition, up to 20% of couples with unexplained infertility are unable to achieve fertilization due to defective interactions of gametes. This latter group may include those with defects in sperm/zona pellucida receptors; in some couples sperm binding occurs at the level of the zona pellucida but without penetration while with the others binding fails to occur.

One of the intrinsic problem of CC/hMG superovulation is prolonged hypersecretion of LH caused by CC which can lead to a degree of luteinization in the preovulatory cycle[11]. Furthermore, overexposure of the developing follicle to LH can lead to failure of implantation ascribed to decreased embryo fitness[15]. This may be due to premature initiation of terminal growth changes in follicle cells and oocytes, similar to those seen at midcycle following LH surge, but not sufficient to provoke follicular rupture [16,17].

The low pregnancy rate (take-home baby,7.4%) for IVF&ET reported in this paper may be due to our inadequate experience in the management of patients stimulation protocol, in vitro culture set up, media used and the postembryo transfer management of patients. However, we are hoping to improve our IVF&ET set up with the induction of GnRH agonist, better laboratory conditions and better management of patients following transfer.

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Perinatal Mortality of Singleton Pregnancy at Nakornpathom Hospital : 1984-1987

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Abstract : *An exploratory research of perinatal mortality was carried out at Nakornpathom Hospital from January 1, 1984 to December 31, 1987. There were 16973 births with a total of 300 perinatal deaths, of which 138 deaths were still-births and 162 were neonatal deaths. The perinatal mortality rate was 17.7 per 1000 births. The main cause of death was due to asphyxia which can be reduced by systematically observing and controlling the progress of labour. Any delay in progress or changes that might be hazardous to mother and fetus should be dealt with promptly. (Thai J Obstet Gynaecol 1990; 2: 7-10.)*

Key words : perinatal mortality, singleton pregnancy

Perinatal mortality rate is an indicator of the quality of obstetric and neonatal cares. It also reflects the socio-economic status of the respective community. Constant availability of perinatal health data on a regular basis would help health planners and economists greatly in setting objectives and monitoring the progress to fulfill the ideal of health for all by the year 2000. The objective of this study was to analyse the basic statistics on the perinatal mortality rate and causes of perinatal death over a four-year period from 1984-1987 at Nakornpathom Hospital. It is hoped that the findings will help to improve the quality of obstetric and neonatal care sevices and at the same time reduce further perinatal mortality and morbidity at Nakornpathom Hospital.

Materials and Methods

Analysis of the data was car-

ried out on records of patients having delivered singleton births at Nakornpathom Hospital from January 1, 1984 to December 31, 1987. The World Health Organization's definition of perinatal mortality is used[1]. 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[2].

Results

During the period of study there were 16973 total births. The yearly data of perinatal deaths and perinatal mortality rate are shown in Table 1. There was a total of 300 perinatal deaths, of which 138 deaths were stillbirths and 162 were in the first week of neonatal life, giving the perinatal mortality rate of 17.7 per 1000 births. The perinatal mortality rate fluctuated between 1981 and 1984 (21.3, 15.0, 15.3 and 19.3 per 1000 births, respectively, Fig. 1). The causes of death were due to birth trauma and intrapartum birth asphyxia (26.0%), specific conditions such as alpha-thalassemia, hypertensive disorders in pregnancy, antepartum hemorrhage, syphilis and meconium aspiration sydrome (22.7%), macerated fetus where there were no definite pathological diagnosis due to severe autolysis of the fetuses (22.3%), prematurity (19.0%) and congenital malformation (10.0%), (Table 2).

Table 1 Perinatal mortality of singleton births, Nakornpathom Hospital, 1984-1987

Years	Births	SB	NND	PMR
1984	4184	33	56	21.3
1985	4413	34	32	15.0
1986	4236	33	32	15.3
1987	4140	38	42	19.3
Total	16973	138	162	17.7

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

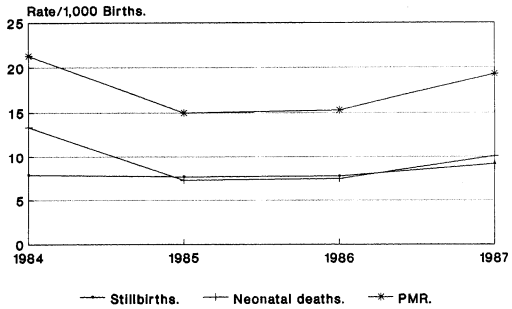

Fig. 1 Percentage mortality of singleton births, Nakornpathom Hospital, 1984-1987

Table 2 Percentage distribution by causes of death, Nakornpathom Hospital, 1984-1987

Causes of death	1984	1985	1986	1987	Total
Asphyxia	30.3	31.8	15.4	25.0	26.0
Specific cond.	12.4	28.8	27.7	25.0	22.7
Maceration	18.0	22.7	22.7	22.5	22.3
Prematurity	25.8	10.6	20.0	17.5	19.0
Cong. malform.	13.5	6.1	9.2	10.0	10.0

Discussion

The perinatal mortality rate at Nakornpathom Hospital was found to fluctuate between 15.0 to 21.3 per 1000 births in the years 1984-1987. When comparing the perinatal mortality rate with other provincial hospitals, it was nearly the same rate, for example at Saraburi Hospital in the years 1983-1987 the perinatal mortality rate was between 19.6 to 24.4 per 1000 births[3]. Other factors that might influence the perinatal mortality rate apart from the obstetric care, socio-economic, physical, cultural and environment of the patient are the method of data collection, for example, only single births were included in this study. Other statistics distorted by various factors, e.g. infants discharged home early with their mothers or transfering of neonates to regional medical hospitals may be some of the factors behind the low perinatal mortality rate.

The main fluctuation in perinatal mortality rate is due to the fluctuation in the neonatal death rate, whereas, the stillbirth rate remains fairly constant. The apparent reduction in perinatal mortality rate was mainly from neonatal death. No postmortem was done in this hospital so it is difficult to define the causes of death with certainty. However, to simplify the causes of perinatal deaths, Wigglesworth's classification was used, to which perinatal deaths can be provisionally assigned and clear implications for clinical management possible. From this study, it was found that preventable causes of death was asphyxia leading to fresh stillbirths or early neonatal deaths. Totally, this accounted for 26.0% and if we consider a birthweight of > 2500 g asphyxia accounted for 43.4% (Table3). In this group, the perinatal mortality rate can be reduced by observing and controlling the progress of labour by using the concept of active management[4], labour graphic records[5], delivery of the infant in good condition with liberal use of caesarean section for preterm infants in breech presentation or transverse lie, and also administration of beta-mimetic drugs and glucocorticoids to the mother prior to preterm labour. Caesarean section rate in this hospital was 10.3%. Any delay in progress or changes that might be hazardous to mother and fetus are promptly dealt with. Adequate resuscitation at birth and good general management in the newborn intensive care unit will also improve the rate of perinatal loss. By this way, the perinatal mortality rate can be reduced to less than 10.0 per 1000 births without

Table 3 Percentage causes of death by birthweight, Nakornpathom Hospital, 1984-1987

Causes of death	Birthweight ≤ 2500 g	Birthweight > 2500 g
Asphyxia	17.4	43.4
Specific cond.	21.4	25.3
Maceration	23.4	20.2
Cong. malform.	9.5	11.1
Prematurity	28.4	0.0

the use of sophisticated equipment such as electronic fetal monitoring and/or ultrasound in the routine care of the mothers[6]. In order to reduce the perinatal mortality rate further the next step after reducing the preventable perinatal death, the macerated stillbirhts should be investigated promptly. The cause of death in this group is unknown but utero-placental insufficiency seems to be the main cause of death especially in high risk pregnancy and can be detected by antepartum monitoring of fetal growth and in cases of suspicion of chronic asphyxia termination of pregnancy has been shown to reduce stillbirth and neonatal death. Intrauterine infection may be the cause of antenatal deaths. In this hospital, antenatal care needs to be improved. Although 75.3% of pregnant women had antenatal care, only 48.8% had 4 or more antenatal visits.

This study may provide some basic data on which decision on appropriate alternative clinical managements as well as to improve facilities can be made at minimal cost.

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Urinary Thromboxane B2 and 11-dehydro-Thromboxane B2 in Normal and Pre-eclamptic Pregnancies

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Abstract: *The production of urinary thromboxane B2 (TXB2) and 11-dehydro-thromboxane B2 (11-dehydro-TXB2), a major urinary metabolite of TXB2, was determined throughout gestation in 25 normotensive pregnant women. These were compared with urinary levels of TXB2 and 11-dehydro-TXB2 in 20 women with mild pre-eclampsia. Urinary TXB2 and 11-dehydro-TXB2 levels did not change with gestation. In normal pregnancies urinary levels of TXB2 (geometric mean 0.66 ng/mg creatinine, 95% CI 0.57 to 0.75) were significantly lower ($p<0.0001$) than those of 11-dehydro-TXB2 (geometric mean 1.02 ng/mg creatinine, 95% CI 0.92 to 1.13). In women with pre-eclampsia, this was reversed in that urinary levels of TXB2 were higher (geometric mean 1.56, 95% CI 1.22 to 1.99) than those of 11-dehydro-TXB2 (geometric mean 0.68, 95% CI 0.52 to 0.87) ($p<0.0001$). TXB2 levels were higher ($p<0.0001$) and 11-dehydro-TXB2 levels were lower ($p<0.004$) in the women with pre-eclampsia than in the controls. This change in metabolism of TXB2 may be the result of an alteration in placental metabolism, since the enzyme responsible for the conversion of TXB2 to 11-dehydro-TXB2 is a placental enzyme. These changes are quite striking, considering that most of the women had mild pre-eclampsia, which settled on bed rest. (Thai J Obstet Gynaecol 1990; 2: 11-17.)*

Key words : urinary thromboxane B2, 11-dehydro-thromboxane B2, pre-eclamptic pregnancy

Pre-eclampsia is still a major cause of obstetric morbidity and mortality. Although its aetiology remains unknown, much recent work has focused on the role of prostaglandins in this disease[1]. Thromboxane A2, a major product of arachidonic acid metabolism in platelets and a powerful

vasoconstrictor inducing irreversible platelet aggregation, is thought to play a major role in the aetiology of pre-eclampsia[2,3]. Thromboxane A2 is labile and concerts rapidly into stable metabolite, thromboxane B2 (TXB2). The major urinary matabolite of TXB2 is 11-dehydro-thromboxane B2 (11-dehydro-TXB2)[4], and thus represents platelet turnover. Although the 11-dehydrogenase is found in the general vasculature, it is also present in the placenta[5], and the overall metabolism of TXB2 may therefore be altered during pregnancy. This prospective study was undertaken to assess urinary TXB2 and 11-dehydro-TXB2 levels throughout normotensive pregnancy. Urinary levels of TXB2 and 11-dehydro-TXB2 were also measured in cases of pre-eclampsia during the third trimester to determine whether this pathology affected TXB2 and 11-dehydro-TXB2 levels.

Materials and Methods

Subjects

Twenty five primigravidae were asked to collect urinary samples at the booking visit, between 16-20 weeks, 20-28 weeks, 28-36 weeks, and between 36 weeks to term and at 1-3 days after delivery to determine normal ranges of TXB2 and 11-dehydro-TXB2 in normal pregnancy. All women were healthy with certain dates confirmed on early ultrasound scans. Those with a previous history of diabetes or renal disease were excluded. These women took no drug (except iron and vitamin supplements), had normal blood pressure throughout gestation and gave birth to healthy infants at 37-42 weeks.

Twenty women with pre-eclampsia were also studied. All had a blood pressure of higher than 140/90 mmHg and proteinuria 1+(Dipstick) during the third trimester of pregnancy. They were entered into the study following the appearance of clinical symptoms of pre-eclampsia. All were admitted to hospital, and 2 received oral antihypertensive drug therapy (alpha-methyldopa); this treatment was started before collection of the first urine sample. Following hospitalisation, blood pressure fell in most patients, such that at the time of urine collection they were barely hypertensive (Table 1).

All infants survived and were discharged with the mothers.

Renal function, as determined by serum creatinine concentrations, was normal in all patients. All had normal blood pressure without proteinuria at 6-week postpartum check up.

No aspirin-like compounds were taken for two weeks prior to or during the collection periods.

Urine collection

Samples (15-20 ml) were collected after voiding and within 2 hours frozen at -20° C until analyzed. Storage did not alter the concentrations of these thromboxanes[4,6].

Metabolite assay

One ml of urine was acidified

to pH 3.0 with formic acid and passed through an ODS cartridge (Sep-Pak, Waters,UK) to extract the prostanoids as described previously[7].

TXB2 levels were determined by an "in-house" RIA, employing TXB2 specific antibody (ICN, Biomedical, UK), [3H]-TXB2 (Amersham, UK).

11-dehydro-TXB2 levels were determined by RIA kit (Amersham, UK). The 11-dehydro-TXB2 antibody had a cross-reactivity of 0.02% of TXB2.

The intraassay coefficient of variation was less than 8% for both assays and the interassay coefficient of variation was 10 and 7% for TXB2 and 11-dehydro-TXB2, respectively. The results of the TXB2 and 11-dehydro-TXB2 measurements are given as ng/mg creatinine, which was assayed by a routine method using quantitative, colometric determination at 500 nm (Sigma Diagnostics, MO, USA).

Statistical analysis

Descriptive parametric statistics were applied after logarithmic transformation to normalize distribution which were then verified using the Shapiro Francia W' test. Normally distributed parametric variables were analyzed by the Student's "t" test, while the Mann-Whitney test were used for nonparametric variables. Change in TXB2 and 11-dehydro-TXB2, (postdelivery level minus the last level during pregnancy) were analyzed by the paired Wilcoxon test.

Results

Clinical characteristics of the study groups are shown in Table 1. The patients in pre-eclamptic group were older than those in the normotensive group. Although gestational age at delivery was similar, mean birth weight in the pre-eclamptic group was significantly less ($p<0.008$) than in the normal group.

No correlation was found between urinary creatinine excretion and gestational age. Urinary creatinine excretion in pre-eclampsia did not differ from normal pregnancy (pre-eclampsia: geometric mean 0.69 mg/ml., 95% CI 0.52 to 0.93, normal pregnancy: geometric mean 0.74 mg/ml, 95% CI 0.66 to 0.84). Levels of urinary TXB2 were significantly higher ($p<0.0001$) in women with pre-eclampsia than in normotensive controls (Table 2). Urinary levels of TXB2 in both groups were unaffected by gestational age, and did not significantly during the three days after delivery. Levels of 11-dehydro-TXB2 in normal pregnancy were found to be significantly higher ($P<0.0001$)than those of TXB2 (Table 2), and were not affected by gestational age. In contrast, the levels of 11-dehydro-TXB2 were significantly lower than those of TXB2 ($P<0.0001$) in the women with pre-eclampsia (Table 2). In the immediate postpartum period levels of urinary 11-dehydro-TXB2 only fell significantly (mean change -0.37, $p=0.009$) in the women who had hypertensive pregnancies. Levels of urinary 11-de-

Table 1 Clinical characteristics of the study groups

	Normal pregnancy	Pre-eclampsia
No. of women	25	20
Age (year)	26.1	31.1*
	(CI 24.4-27.8)	(CI 28.6-33.6)
Parity:		
Nulliparous	25	18
Parous	0	2
Blood pressure:		
Systolic (mmHg)	112	139*
	(CI 110-114)	(CI 133-143)
Diastolic (mmHg)	69.8	90.6*
	(CI 68-71)	(CI 87-94)
Mode of delivery:		
Vaginal	22	16
Caesarean section	3	4
GA at delivery (week)	39.4	38.5
	(CI 38.8-39.9)	(CI 37.5-39.5)
Birth weight (Kg)	3.33	2.99**
	(CI 3.24-3.42)	(CI 2.76-3.22)

*p <0.001, **p <0.008 (unpaired t-test)
#Blood pressure at time of urine collection
CI = 95% confidence interval
GA = Gestational age

Table 2 Urinary excretion of TXB2, 11-dehydro-TXB2, and the TXB2:11-dehydro-TXB2 ratio in normotensive and pre-eclamptic women

	Normotensive women		Pre-eclampsia	
	Pregnant	Postpartum	Pregnant	Postpartum
Urinary TXB2				
(ng/mg Cr)				
geometric mean	0.66	0.89	1.56*	1.27
95% CI	0.57-0.57	0.61-1.29	1.22-1.99	0.91-1.79
Urinary 11-deH-TXB2				
(ng/mg Cr)				
geometric mean	1.02	0.89	0.68**	0.31
95% CI	0.92-1.13	0.58-1.36	0.52-0.87	0.21-0.43
Urinary TXB:11-deH-TXB2				
geometric mean	0.64	0.93	2.51*	3.81
95% CI	0.53-0.77	0.55-1.58	1.85-3.39	2.90-5.02

*P<0.0001, **P=0.004, compared to normotensive women (Mann-Whitney test)
Cr = Creatinine, TXB2 = Thromboxane B2, 11-deH-TXB2=11-dehydro-TXB2
CI = Confidence interval

Table 3 Accuracy of an elevated urinary TXB2:11-dehydro-TXB2 ratio of greater than 1.3 on consecutive occasions in identifying pre-eclampsia

	Urinary TXB2:11-dehydro-TXB2	
	<1.3	≥ 1.3
Normotensive women (n)	17	8
Pre-eclampsia (n)	1	19

Sensitivity 95%, Specificity 68%
Positive predictive value 70%
Negative predictive value 94%
Kappa index 0.61

hydro TXB2 were lower in women with pre-eclampsia than in women with normotensive pregnancies (Table 2).

The ratio of TXB2:11-dehydro-TXB2 was calculated and found to be very significantly different ($p<0.0001$) between women with pre-eclampsia and women with normotensive pregnancies (Table 2). The sensitivity and specificity of a TXB2:11-dehydro-TXB2 ratio of ≥ 1.3 on two consecutive measurements as a retrospective test for pre-eclampsia were calculated to be 95% and 68% respectively (Table 3).

Discussion

The analysis of urinary metabolites represents a noninvasive approach to the assessment of thromboxane biosynthesis in vivo and avoids potential artefacts associated with plasma measurements[8,9].

In normal pregnancy TXB2 and 11-dehydro-TXB2 concentrations did not change with gestation and the levels of 11-dehydro-TXB2 were higher than TXB2, confirming that 11-dehydro-TXB2 is the major urinary metabolite of TXB2 during pregnancy as well as in the non-pregnant state[4]. The major source of thromboxane in pregnancy is from platelet activation[8] and only a minority from the placenta[10] or the renal glomeruli[11].

The lack of a significant difference in urinary levels of thromboxane metabolites 1-3 days postpartum was not unexpected, since any change in platelets function during pregnancy would be expected to persist until a completely new population of platelets had been synthesised, which would require about 10 days[8]. Urinary TXB2 and 11-dehydro-TXB2 are known to have returned to pre-pregnancy levels 6 weeks postpartum [6,8].

It has been found that TXB2 levels in pre-eclamptic women were higher than in normotensive women[5, 6]. However, the levels of 11-dehydro-TXB2 in pre-eclamptic women have

not been clearly defined. Fizgerald et al[5] found that both plasma and urinary 11-dehydro-TXB2 levels in severe pre-eclampsia were elevated. In this study of relative mild pre-eclamptics urinary 11-dehydro-TXB2 levels in pre-eclamptic women were lower than in women with normal pregnancies. This was not due to reduced renal clearance of 11-dehydro-TXB2 since the urinary creatinine concentrations in both groups were similar. The enzyme responsible for the conversion of TXB2 to 11-dehydro-TXB2 is placental enzyme[5], so the placental damage present in pre-eclampsia may have decreased the activity of the enzyme. This is supported by the finding that although TXB2 levels were increased in the women with pre-eclampsia, 11-dehydro-TXB2 levels were decreased. This is consistent with placental damage inhibiting the activity of the 11-dehydrogenase enzyme. The finding of significantly decreased urinary levels of 11-dehydro-TXB2 after delivery, without any changes in TXB2 levels, also supports the role of a placental enzyme in the production of 11-dehydro-TXB2.

Despite the decrease in 11-dehydro-TXB2 levels, total thromboxane metabolite production (TXB2 + 11-dehydro-TXB2) was still higher in the women with pre-eclampsia, which has been reported elsewhere[2,3]. This elevation in platelets aggregration in pre-eclampsia is consistent with the known beneficial effects of low dose aspirin in pre-eclampsia[12-14].

Using a TXB2:11-dehydro-TXB2 ratio of $\geq$ 1.3, a sensitivity of 95% and specificity of 68% was obtained, although this is a retrospective analysis. The Kappa index of 0.61 suggests that this is not a chance finding. The clinical usefulness of this measurement in the prediction of pre-eclampsia needs to be assessed in a longitudinal study in pregnant women during the second and third trimesters.

In conclusion, this study documents normal levels of urinary TXB2 and 11-dehydro-TXB2 throughout pregnancy. In normal pregnancy 11-dehydro-TXB2 is the major metabolite for thromboxaneA2,whereas,in the women with pre-eclampsia the opposite applied and TXB2 predominated. The ratio of urinary TXB2 to 11-dehydro-TXB2 concentration might be a predictive test for pre-eclampsia, though further work is needed.

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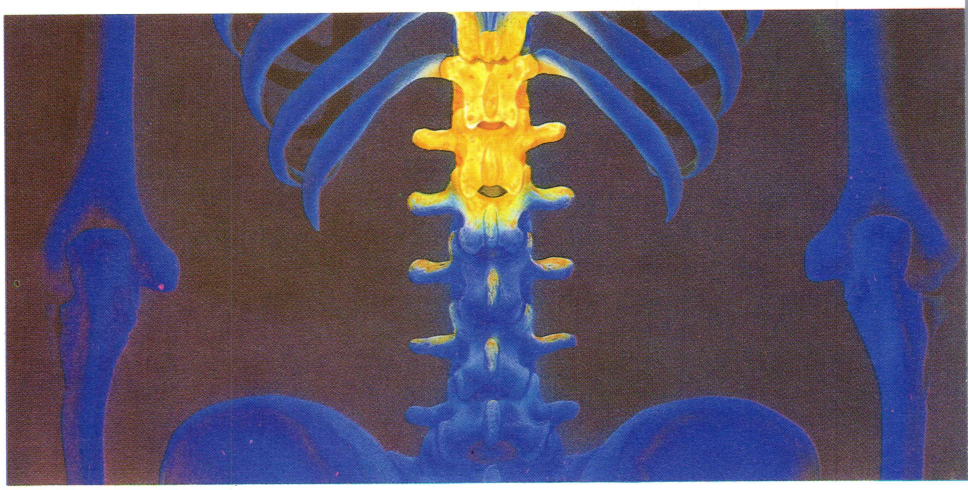

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The Efficacy of Spectinomycin, Norfloxacin and Ciprofloxacin in the Treatment of Uncomplicated Gonorrhoeae

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Abstract: *This is a prospective study comparing spectinomycin, norfloxacin and ciprofloxacin in the treatment of uncomplicated gonorrhoeae in female patients. Of 461 patients, there were 169 patients (36.7%) who had PPNG strains. The cure rate was 98.4% in the spectinomycin group (n=128), 98.6% in the norfloxacin group (n=282) and 100% in ciprofloxacin group (n=45) whether the infection was caused by PPNG or non-PPNG.(Thai J Obstet Gynaecol 1990; 2:.19-22.)*

Key words : uncomplicated gonorrhoeae, spectinomycin, norfloxacin, ciprofloxacin

In the areas where penicillinase producing Neisseria gonorrhoeae (PPNG) strains are highly prevalent, the drugs for treatment of gonococcal infection should be highly effective for both PPNG and non-PPNG strains. The recommended treatment for uncomplicated gonorrhoeae should be in the group of spectinomycin, cephalosporins and quinolone derivatives such as norfloxacin, ofloxacin and ciprofloxacin which have been reported to be highly effective[1]. At the outpatient Department of Obstetrics and Gynaecology, Ramathibodi Hospital, the drugs which were recommended for treatment of uncomplicated Neisseria gonorrhoeae should give the cure rate of at least 95%. Spectinomycin was first used routinely for the treatment of uncomplicated gonorrhoeae. Although spectinomycin is the drug that produces an acceptable cure rate and is recommended in the treatment of PPNG strains, PPNG strains resistant to spectinomycin have been reported in many parts of the world[2-5]. Quinolone derivatives was an alternative treatment and is a single-dose oral administration. At the Department of Obstetrics and Gynaecology, Ramathibodi Hospital, norfloxacin was first

used in early 1986 and ciprofloxacin was first used in late 1988. Cephalosporins i.e. cefotaxime was used as the second line drug to treat cases resistant to spectinomycin, norfloxacin and ciprofloxacin[6,7]. The objectives of this study were to evaluate the efficacy and side effects of spectinomycin, norfloxacin and ciprofloxacin in the treatment of uncomplicated gonorrhoeae in female patients.

Materials and Methods

A prospective study was conducted at the sexual health clinic, Department of Obstetrics and Gynaecology, Ramathibodi Hospital, between January 1,1986 and December 31,1989. The details were obtained from the medical records. There were 461 female patients with the diagnosis of uncomplicated gonorrhoeae. The diagnosis was established by a positive culture from the central laboratory. These 461 patients were treated with one of three regimens. Regimen 1, patients received 2g of spectinomycin intramuscularly. Regimen 2, patients received 800mg of norfloxacin orally. Regimen 3, patient received 250mg of ciprofloxacin orally and the same regimens were applied to their sexual partners[1]. In case of failure to the first treatment, patients received 500 mg cefotaxime intramuscularly after 1g probenecid orally. A repeated culture was done between day 3-10 after treatment from the urethra and cervix. The specimens were inoculated on the Thayer-Martin media and incubated at 35°C in an atmosphere of carbon dioxide. The patients were considered cured if the results of the culture were negative in all sites. If there was a positive culture in one or the other site then the treatment was considered to have failed and cefotaxime was prescribed and the patient was seen again 7 days later for culture. The efficacy was expressed in term of cure rate by culture. The patients were then asked to abstain from sexual intercourse and were asked at the follow-up visits about side effects such as drowsiness, nausea, vomiting and pain at the injection site.

Results

Of 461 female patients who entered into the study, there were 169 patients who had PPNG strains. The prevalence of PPNG strains in each year varied from 33.6 to 39.5%. The overall prevalence was 36.7% (Table 1). The cure rate was 98.4% in the spectinomycin group (n=128), 98.6% in the norfloxacin group (n=282) and 100% in the ciprofloxacin group (n=45) (Table 2). The cure rate in the spectinomycin group for PPNG varied from 92.3 to 100% in the four-year period. The average cure rate was 96.6%. In the non-PPNG the cure rate was 100%. The cure rate in the norfloxacin group for PPNG varied from 94.1 to 100% . The average cure rate was 96.8%. In the non-PPNG the cure rate varied from 98.2 to 100%. The average cure rate was 99.5%. The cure rate in the ciprofloxacin group

Table 1 The prevalence of PPNG and non- PPNG

Year / Strains	1986 No.	%	1987 No.	%	1988 No.	%	1989 No.	%	Total No.	%
PPNG	48	38.4	45	39.5	43	33.6	33	35.1	169	36.7
Non-PPNG	77	61.6	69	60.5	85	66.4	61	64.9	292	63.3
Total	125	100	114	100	128	100	94	100	461	100

Table 2 Efficacy of spectinomycin, norfloxacin and ciprofloxacin

Drugs	No.of cases	Cure	%
Spectinomycin	128	126	98.4
Norfloxacin	282	278	98.6
Ciprofloxacin	45	45	100.0

Table 3 Efficacy of spectinomycin, norfloxacin and ciprofloxacin in PPNG strain

Drugs / Year	1986 Cure No.	%	Failed NO.	%	1987 Cure NO.	%	Failed NO.	%	1988 Cure NO.	%	Failed NO.	%	1989 Cure NO.	%	Failed NO.	%	Total Cure NO.	%	Failed NO.	%
Spectinomycin	24	96.0	1	4	14	100	0	0	12	92.3	1	7.7	6	100	0	0	56	96.6	2	3.4
Norfloxacin	22	95.7	1	4.3	31	100	0	0	22	95.7	1.	4.3	16	94.1	1	5.9	91	96.8	3	3.2
Ciprofloxacin	0	0	0	0	0	0	0	0	7	100	0	0	10	100	0	0	17	100	0	0
Total	46	95.8	2	4.2	45	100	0	0	41	95.3	2	4.7	32	97.0	1	3.0	164	97.0	5	3.0

Table 4 Efficacy of spectiomycin, norfloxacin and ciprofloxacin in non- PPNG strain

Drugs / Year	1986 Cure No.	%	Failed NO.	%	1987 Cure NO.	%	Failed NO.	%	1988 Cure NO.	%	Failed NO.	%	1989 Cure NO.	%	Failed NO.	%	Total Cure NO.	%	Failed NO.	%
Spectinomycin	30	100	0	0	14	100	0	0	15	100	0	0	13	100	0	0	72	100	0	0
Norfloxacin	47	100	0	0	54	98.2	1	1.8	62	100	0	0	28	100	0	0	191	99.5	1	0.5
Ciprofloxacin	0	0	0	0	0	0	0	0	8	100	0	0	20	100	0	0	28	100	0	0
Total	77	100	0	0	68	98.6	1	1.4	85	100	0	0	61	100	0	0	291	99.7	1	0.3

was 100% in both PPNG and non-PPNG groups (Tables 3, 4). There were no side effects in the ciprofloxacin group, but one case in the spectinomycin group had severe pain at the injection site and 6 cases in the norfloxacin group had nausea and drowsiness. All side effects were minimal and did not warrant any treatment.

Duscussion

The efficacy of various regimens including spectinomycin and quinolone derivatives, i.e. norfloxacin and ciprofloxacin for the treatment of uncomplicated gonorrhoeae whether the infection was caused by PPNG or non-PPNG strains showed little significant variation in therapeutic

efficacy[8,9]. The overall cure rates were 98.4% for spectinomycin, 98.6% for norfloxacin and 100% for ciprofloxacin. One case in the spectinomycin group had severe pain at the injection site and 6 cases in the norfloxacin group had nausea and drowsiness but none in the ciprofloxacin group. There were no side effects in the ciprofloxacin group possibly because the number of cases was few and it is too early to conclude that ciprofloxacin had no side effects. In this study, there was one case in the non-PPNG group that developed a resistance to norfloxacin at the dosage of 800mg but was sensitive to spectinomycin and ciprofloxacin. There were 5 cases in the PPNG group that developed resistance, 3 in the norfloxacin and 2 in spectinomycin groups. This failure in treatment suggested that antibiotics should be used appropriately in the treatment of uncomplicated gonorrhoeae. There is also a need to find an alternative treatment and keep some antibiotics such as cephalosporins in reserve for some resistant cases. In this study,6 failures were treated effectively by using cefotaxime plus pro-benecid. There was no difference in the cure rates between spectinomycin and quinolone derivatives, i.e. norflo-xacin and ciprofloxacin but the advantage of quinolone derivatives over spectinomycin is in its rapid absorption following oral administration, and also it costs less and is easier to administer than spectinomycine. Using the regimen described here norfloxacin and ciprofloxacin are, therefore, safe and effective drugs in the treatment of uncomplicated gonorrhoeae caused by both PPNG and non-PPNG. Both are alternative drugs against gonococcal infection with low costs and are easy to administer.

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Management of Patients with Mild Dysplasia on Cervical Cytology

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Abstract : *The study was carried out to find out the proper management of patients with mild dysplasia diagnosed on cervical cytology.*

Two hundred and twenty four patients with mild dysplasia on the initial cervical cytology and in whom colposcopy or other means for histopathologic taking had been performed within 3 months after taking the initial Pap smears between September 1978 and March 1988 were the subjects to be evaluated. Three hundred and sixty six (62%) of the 590 women with mild dysplasia on the initial Pap smears were lost to follow-up.

Thirty seven (16.5%) of 224 patients had cervical intraepithelial neoplasia (CIN) grade II or worse on histology and one patient had an invasive carcinoma. Mean age of the patients with CIN was 30 years and mean age was higher in association with the severity of CIN. The parity had no relationship with the severity of CIN.

Although only 16.5% of the patients had more severe histological diagnosis of the uterine cervix than those diagnosed by cervical cytology, it was clear that there was one case of invasive carcinoma and a large number of patients had been lost to follow-up. It is recommended that all patients with a smear report of mild dysplasia should be subjects for colposcopy. (Thai J Obstet Gynaecol 1991;2:23-27.)

Key words : management of mild dysplasia, cervical cytology

The decline in morbidity and mortality rates for invasive squamous cell carcinoma of the cervix over the past several decades attests to the importance of identifying women who are at a greater risk for developing this desease, examining them, and treating the condition as early as possible. Today, colposcopy, used in conjunction with cytology and histopathology, is a valuable diagnostic technique used throughout the world. Proper evaluation, treatment, and follow-up of Pap smears showing mild

dysplasia has been controversial. Some authors recommended immediate colposcopy for patients with an initial Pap smear of mild dysplasia because of a poor correlation between cytology and histopathology of the uterine cervix[1-6]. Other authors have suggested that these patients should be initially managed conservatively because of a high regression rate to a normal repeated smear[7-9]. We, therefore, intended to evaluate the histopathology of the uterine cervix whose initial cytology was mild dysplasia and to assess for risk factors associated with histopathology worse than CIN II.

Materials and Methods

All patients with mild dysplasia on the initial Pap smear at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University from September 1978 to March 1988 were studied. All patients had histopathology of the uterine cervix by colposcopic directed biopsy, naked-eye punch biopsy, cervical conization or hysterectomy within 3 months after the initial Pap smear. The grading classification of our cytology laboratory is a modification between WHO[10] and Papanicolaou classifications. Data analysis consisted of 1) descriptive statistics to describe the characteristics of the subjects, and 2) inferential statistics to compare the characteristics of the subjects under different subgroups. Analysis of variance and *Student's t-test* were used as appropriate. Statistically significant difference was determined when p value was less than 0.05

Results

There were 590 patients with mild dysplasia on the initial Pap smear during the study period, 224 of which were available for study. The means for obtaining cervical histopathology are shown in Table 1. The cervical histopathology of all 224 patients is shown in Table 2, 16.5% of these women had cervical histopathology worse than mild dysplasia. Diagnostic conization was performed on 17 patients, 13 patients for CIN III after naked-eye punch biopsy, 2 patients for unsatisfactory colposcopic finding and 2 patients for discrepancy between cytology and histology. The final treatments for these 224 patients are shown in Table 3 which noted that 22% of these patients required further treatment. The range of ages of patients with CIN I and CIN II was 30-34 years while that of patients with CIN III was 35-39 years. The mean ages of patients with CIN I, CIN II and CIN III were 29.9±5.5, 32.0±7.4 and 36.7±9.9 years respectively. The means parity of patients with CIN I, CIN II and CIN III were 2, 2 and 3 respectively. The means parity of patients with CIN I, CIN II and CIN III were 2.1±0.9, 2.5±1.1 and 3.1 ± 0.8 respectively. There were no statistically significant difference between patients with histopathology of CIN II or worse and less severe than CIN II

Table 1 Methods of final histologic taking

Methods	No.	Per cent
Colposcopically directed biopsy	67	29.9
Cervical punch biopsy	12	5.4
Cervical conization	17	7.6
Hysterectomy specimen	16	7.1
Normal colposcopicfinding without colposcopically directed biopty	12	50.0
Total	224	100.0

Table 2 Colposcopic results and/or histopathology of the cervix

Histopathology	No. of Patients	Per cent
Unremarkable	19	8.5
Inflammation	38	16.9
CIN I	18	8.1
CIN II	12	5.4
CIN III	24	10.7
Invasive carcinoma stage IB	1	0.4
Normal colposcopic finding	112	50.0
Total	224	100.0

Table 3 Final treatment

Treatment	No. of Patients	Per cent
No treatment	48	21.4
Antibiotics	127	56.7
Cryosurgery	8	3.6
Therapeutic conization	3	1.4
Simple hysterectomy	37	16.5
Radical hysterectomy & pelvic node dissection	1	0.4
Total	224	100.0

Table 4 Comparison between patients with CIN II or worse and less severe than CIN II

Histopathology	Mean Age ± SD (Range in years)	Mean Parity ± SD (Range)
CIN II or worse	34.2 ± 8.6 (21-68)	2.7 ± 2.0 (0-12)
Less severe than CIN II	33.3 ± 10.0 (18-69)	2.2 ± 1.8 (0-9)
p value	NS (p>0.05)	NS (p>0.05)

NS = Not significant

in terms of mean age and parity, Table 4.

Discussion

This study reveals the presence of CIN and invasive cervical carcinoma in women attending a colposcopy clinic because of mild dysplasia on Pap smears. Sixteen and a half per cent of these patients had CIN II or worse on histology, despite the fact that only 5.1% had persistent mild dysplasia and only 3.8% had moderate dysplasia or worse on the repeat smear at the time of colposcopy. These patients required further appropriate treatment either cryosurgery, conization, hysterectomy or even radical hysterectomy. This data is not unique. In other studies, CIN II or worse was found in 49% to 69% of patients with mild dysplasia on cervical smears[3,4]. Sandmire et al[11] found that 20% of their patients whose initial smears were atypical had CIN III or worse, and in 55% of the patients with CIN III or worse the smear never became more severe than atypical. Seven of these women had invasive

cancer[11]. In a large British study, an initial Pap smear of mild dysplasia, 13% subsequently had a histological diagnosis of CIN or worse, 13% continued to have dyskaryotic smears and 51% had normal or atypical smears[12]. These authors emphasized the need for further investigation of all women with dyskaryosis regardless of grades[3,4,11,12]. It is clear that patients whose smears contain mild dyskaryotic cells are at a much higher risk of having cervical intraepithelial neoplasia or worse than women whose smears are normal[5,13].

The data from our study cannot demonstrate the association between age or parity with CIN II or abnormal cervical histopathology. Therefore, age and parity cannot be used as risk factors for the presence of CIN II or worse. The presence of cases of CIN and invasive carcinoma together with the high rate of loss to follow-up in patients with mild dysplasia on cervical cytology suggest that further immediate action should be taken rather than follow-up in these patients. Women whose cervical smears show dyskaryosis of any degree, even if mild dysplasia, should be refered for colposcopy. If a normal colposcopic finding is found, and a repeat smear is reported as being negative further confirmatory smear 6 months later would be prudent.

Concerning the limitation of this study, the prevalence of CIN II or worse on histology was less than what we had expected. This factor might decrease that accuracy of the prevalence of CIN II or worse in this study, but does not affect the conclusion of our study.

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Prognostic Factors for Survival after Surgery for Early Stages Cervical Cancer

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Abstract : *Two hundred and forty-nine consecutive patients with clinical stage I and IIA carcinoma of the uterine cervix who underwent primary radical hysterectomy and pelvic lymphadenectomy between January 1976 and December 1988 were evaluated for prognostic factors for survival. Univariate analysis, history of smoking, weight of the patients, FIGO staging, surgeons and surgical techniques, histology, lymph nodes status, lesion diameter and recurrent status were the significant factors in death rate. When survival analysis was performed, recurrent status, FIGO staging and lesion diameters remained significant for both corrected and overall survival rates. For preoperative selection of the patients, those with FIGO stage II and tumour diameter 2-4 cm were associated with a less favourable prognosis. (Thai J Obstet Gynaecol 1990; 2: 29-36.)*

Key words : prognostic factors for survival, early stage cervical cancer

Carcinoma of the uterine cervix is the most common gynaecological malignancy in Thailand and is the second most common cancer for the Khon Kaen female population[1,2]. Improvement in early diagnosis and treatment has been achieved over the last two decades. Survival rates in patients whose tumours are confined in the cervix (Stage IB, IIA) treated by both radiotherapy and surgery have remained constant between 82-90% in the past few years. It has been recognized for some time that prognostic factors for survival after surgery are recurrent status[3], lymph node metastasis[4,5-14], tumour size[9,12-13], stages of the disease[9,12-13], depth of stromal invasion[3,19], extracervical extension[3,19-22], histological types[3,5,6,13,19-22], lympho-vascular spreading[9,21,23,24], age and weight of the patients[12,13,15,17] and the use of adjuvant therapy[2]. In order to improve survival rates in patients with early cervical cancer, prognostic factors must be identified.

Materials and Methods

Between January 1, 1976 and December 31, 1988, 249 consecutive patients with FIGO stages IA, IB and IIA cervical carcinoma were operated on by radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University. Clinical staging was done according to the International Federation of Gynaecology and Obstetrics (FIGO) for all patients by gynaecological oncologists and radiotherapists. The operative precedures were done according to Piver's type III extended hysterectomy[5]. Patients with tumour involvement of pelvic lymph nodes, surgical margins and parametria were sent for additional radiotherapy.

Epidemiological data, tumour description, parametria involvement, pelvic lymph nodes status, morphometric data, histological diagnosis and follow-up data were recorded by the staffs of the Division of Gynaecological Oncology and the hospital-based cancer registry of the Cancer Unit, Faculty of Medicine, Khon Kaen University. The follow-up period ranged from 2 to 12 years. All variables were first analyzed for significant relationship to death rate by *chi-square* and Mann-Whitney tests. All significant variables were then analyzed for survival by Kaplan-Meier product limit estimation with log-rank test[26]. Cox' s proportional hazard model[27] was used for the most significant variables for survival. Algorythm for preoperative prediction were then established.

Table 1 Prognostic factors for survival after radical hysterectomy in cervical cancer

1.	Recurrence
2.	Lymph nodes status
3.	Tumour size
4.	Stage of the disease
5.	Depth of stromal invasion
6.	Extracervical extension
7.	Histological type and grading
8.	Lympho-vascular spreading
9.	Status of the surgical margin
10.	Thickeness of uninvolved fibromuscular stroma
11.	Age of the patients
12.	Interval from the previous follow-up examinations
13.	Location of the lesion within the cervix
14.	The use of adjuvant therapy
15.	Lesion type
16.	Weight

Table 2 Univariate analysis of prognostic factors for survival after radical hysterctomy for cervical cancer

1.	Recurrence
2.	Stage of the disease
3.	Tumour size
4.	Lesion type
5.	Histological type
6.	Uterine size
7.	Persistene of left ovary
8.	Smoking
9.	Weight
10.	Surgeon

Results

Univariate analysis

All variables from previous reports were analyzed by using death

rate as the dependent variable (Table 1) and only 10 variables were still significant (Table 2). From the Kaplan-Meier product limit estimation only recurrence status, FIGO stages and lesion diameter were still significant for both corrected and absolute survivals (Table 3).

Table 3 Survival analysis of patients after radical hysterectomy for cervical cancer

Prognostic factors	Categories	Absolute survival		Corrected survival	
1. Recurrence	No	86.54		100.00	
	Yes	15.64	P=0.0000	15.64	P=0.0000
2. Stages	1A	100.00		100.00	
	1B	82.53	P=0.0020	91.04	P=0.0400
	IIA	0.00		50.51	
3. Lesion size	< 2 cm	79.00		91.91	
	2-4 cm	77.59	P=0.0185	81.84	P=0.0006
	> 4cm	75.00		75.00	
4. Lesion type	No gross lesion	100.00			
	Polypoid	87.66			
	Ulcer	77.01	P=0.36		
	Cauliflower	71.13			
	Infiltrative	47.41			
5. Histology	No residual	83.33		83.33	
	Squamous	74.32		86.63	
	Adeno.	90.61	P=0.38	96.97	P=0.36
	Adenosquamous	100.00		100.00	
6. Uterine size	≤ 8 cm	91.51		97.67	
	> 8 cm	92.10	P=0.81	93.15	P=0.38
7. Persistence left ovary	Yes	86.27		86.27	
	No	94.08	P=0.42	97.66	P=0.32
8. Smoking	Yes	74.33		86.42	
	No	100.00	P=0.226	100.00	P=0.051
9. Weight	< 50 Kg	100.00		100.00	
	> 50 Kg	92.94		93.94	P=0.021
10. Surgeons	S1	78.00		83.20	
	S2	86.06		90.30	
	S3	100.00		100.00	
	S4	100.00	P=0.180	100.00	P=0.80
	S5	37.50		100.00	
	S6	60.00		100.00	

Figure 1 shows the overall survival rates of the patients with 76.58% absolute survival and 88.08% corrected survival rates. Figure 2 shows the overall absolute survival rates according to recurrent status. Those who had no recurrence had 86.54% survival rate while those who had recurrence had only 15.64% survival rate. Figure 3 shows the 100% overall corrected survival rate for those who had no recurrence and 15.64% corrected survival rate for those who had recurrence. Figure 4 and Figure 5 show the overall absolute survival rates according to FIGO stages with 100% and 0% for stages IA, IB and IIA respectively. Figure 6 and Figure 7 show the overall absoulte survival rates of 79%, 77.59% and 75% for those who had a lesion diameter of less than 2 cm, between 2-4 cm and more than 4 cm respectively. For corrected survival, the survival was 91.91%, 81.84% and 75% for those who had a lesion diameter of less than 2 cm, between 2-4 cm and more than 4 cm respectively.

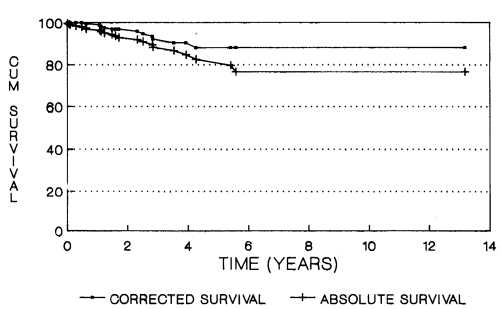

Fig. 1 Survival analysis of patients after radical hysterectomy

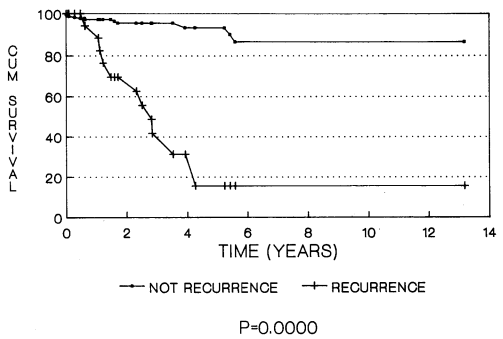

Fig. 2 Absolute survival according to recurrence status

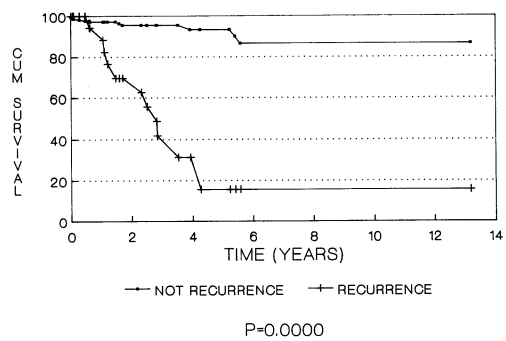

Fig. 3 Corrected survival according to recurrence status

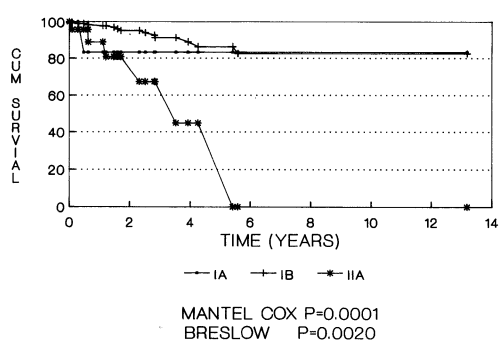

Fig. 4 Absolute survival rates according to FIGO stages

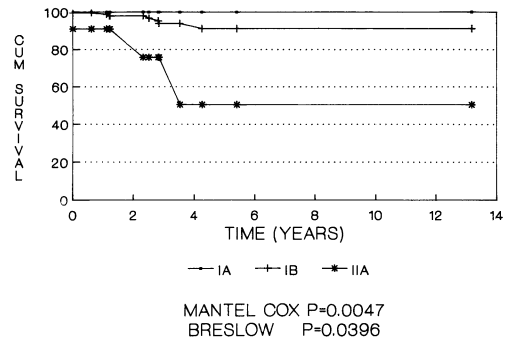

Fig. 5 Corrected survival according to FIGO stages

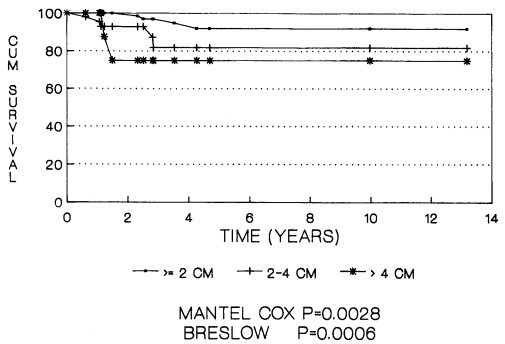

Fig. 7 Corrected survival according to lesion's diameter

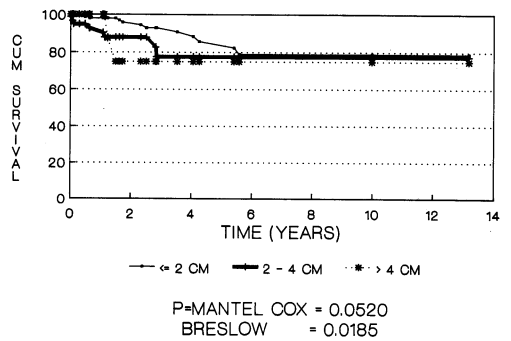

Fig. 6 Absolute survival rates according to lesion's diameter

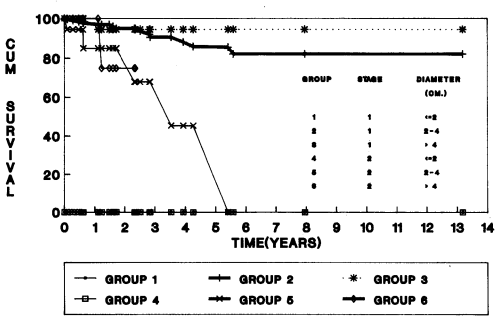

Fig. 8 Grouping of prognostic factors for survival after radical hysterectomy

With Cox's proportional hazard model, only recurrence status and FIGO stages were the most significant prognostic factors for survival. Preoperative grouping of patients was done for FIGO stages in combination with tumour diameters (Figure 8). It was shown that when the patients were grouped into 6 groups the most fovourable outcome was those who had stage I without lesion diameter distinction.

Discussion

After radical hysterectomy and pelvic lymphadenectomy, recurrent rate from 10% to 20% is generally expected. The proposed mode of recurrence is the regrowth of the viable cancer cells which were left behind at the time of surgery. Once recurrence occurs, the prognosis of the patients is poor even though several modes of therapy were given. Only 15.64% of

patients survived 5 years, compared to 86.54% for those without recurrence. The risk factors for recurrence in this series was reported[24].

FIGO staging has been routinely used as the classification of the disease for planning of treatment and prediction of the outcome. Lee et al[13] found the absolute 5-year survival rates for stage IB, IIA and IIB to be 86.5%, 71.7% and 60.1% respectively. This series obtained a very poor rate for stage IIA, the patients survived only 2 years.

Tumour size has been observed to be one of the important factor for recurrence and survival in patients who underwent radical hysterectomy and pelvic lymphadenectomy. It was also reported to be the important prognostic factor in radiated patients as confirmed by Patanaphan et al[15]. Burghardt[5] showed the 5-year survival rate decreased correspondingly with the tumour size which he expressed in term of so-called quotient. The 5-year survival rate of 88.9% was observed in the quotient of 0% to 20% while the rate dropped to 58.9% in the quotient of 80% or more. He also confirmed the tumour size to be the most important prognostic criteria and best suited for patient classification. In multivariate analysis of risk factors in stage I adenocarcinoma, Kilgore et al [17] found that clinical stage and lesion size were the most important prognostic factors for recurrence and survival. In this study it was significant by univariate analysis both for absolute and corrected survival.

The rest of the variables were taken into account for follow-up and further study for prognostic factors for survival and recurrence. For high risk patients who had involvement of cancer at lymph nodes, surgical margins and parametria were given radiotherapy and appeared to be nonsigniticant variables after analysis. Noguchi et al[6] reviewed 627 cases of early stage cervical cancer who underwent Okabayashi radical hysterectomy from 1950 to 1984 and found that lymph nodes metastasis correlated with clinical stage, depth of stromal invasion and involvement of the cancer to parametria, vagina and uterine body. Fuller et al[9] also found the incidence of nodal metastasis increased with the increase of tumour size, tumour grade, and depth of invasion into the cervix.

The two preoperative variables, FIGO stages and lesion size were grouped together and the worse prognosis was found in those who had stage II and lesion diameter 2 to 4 cm. Those who had stage I disease had a better prognosis than stage II and it was not related to lesion size.

From this analysis, it is confirmed that clinical staging as described by FIGO is still useful for preoperative planning in early stage cervical cancer.

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Cephalothoracopagus Syncephalus : A Case Report and Literature Review

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Abstract : *Reports of cephalothoracopagus conjoined twins have appeared rarely in the scientific literatures. At Chulalongkorn Hospital, this malformation is rare with an incidence of one in eight sets of conjoined twins. A case of cephalothoracopagus conjoined twins is presented. Mechanism of conjoining and type of cephalothoracopagus are discussed. (Thai J Obstet Gynaecol 1990; 2: 37-42.)*

Key words : cephalothoracopagus syncephalus, conjoined twins, case report

One of the most interesting congenital malformations is conjoined twins. Since the first reported case, conjoined twins have been the object of curiosity of laymen and doctors alike. The rarity and unusual appearance of the malformation contribute to the fascination. Although the diagnosis is most often missed until labour ensues, conjoined twins are occasionally diagnosed antenatally on the basis of certain radiologic criteria and ultrasonographic findings. Conjoined twins occassionally cause delivery dilemmas for the obstetricians.

The cephalothoracopagus variety is particularly rare. A case of cephalothoracopagus conjoined twins is presented.

Case Report

A 29-year-old Thai woman, gravida 3, para 2-0-0-2, who experienced an uneventful pregnancy, had a history of spontaneous labour beginning 4 hours prior to admission. She had received no prenatal care. Her last menstrual period was unknown. The previous two children were normal and there was no history of twins. She did not smoke cigarettes nor drink alcohol. During the pregnancy she had not taken iron supplement and vitamins. She had an unremarkable medical history. On her way to the hospital, she delivered vaginally in the taxi, with cephalic presentation of stillborn conjoined twins.

External Appearances

The twins had a combined weight of 1420 g. Physical examination showed female twins conjoined anterolaterally at the head and thorax, with separate torsos below the umbilicus and with four arms and legs. The twin's head was large ovoid, with two eyes, one nose and one mouth, all facing forward. There were four ears, one low-set ear on either cheek and two opposing ones at the back of the head opposite the facial features. The conjoined twins had two trunks that opposed each other, joined from a single neck and extended to a shared umbilicus. There were separate pelves, four lower extremities and four upper extremities despite the fused trunk. Complete female external genitalia were present in each body. There were no anomalies of the extremities (Figures 1,2).

The thorax and abdomen are fused, meeting with a single umbilical

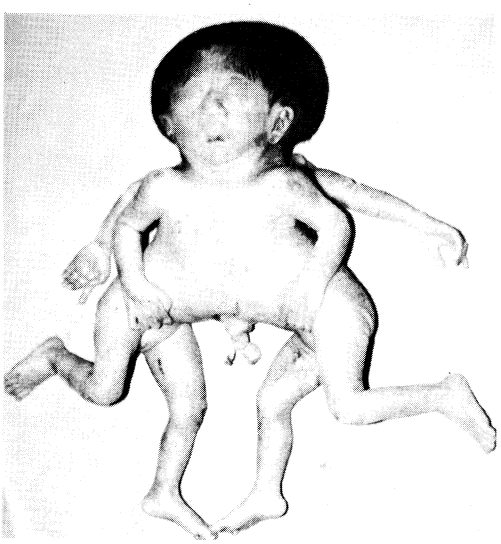

Fig. 1 Anterior view of conjoined cephalothoracopagus twins showing the common ovoid head, two widely spaced eyes, single nose and mouth and low-set ears.

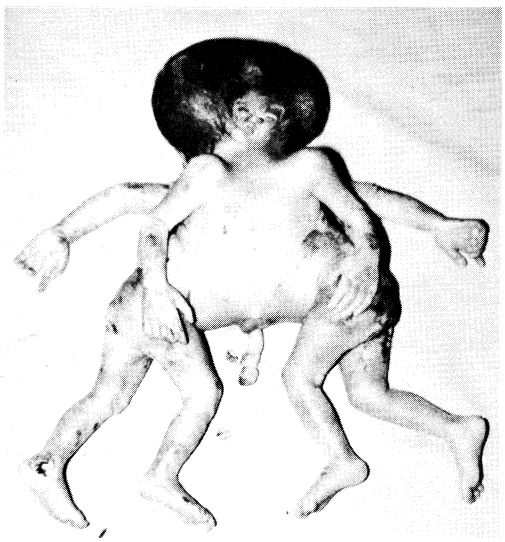

Fig. 2 Posterior view of conjoined cephalothoracopagus twins showing two ears separated by 2 mm were present on the opposite side of the face.

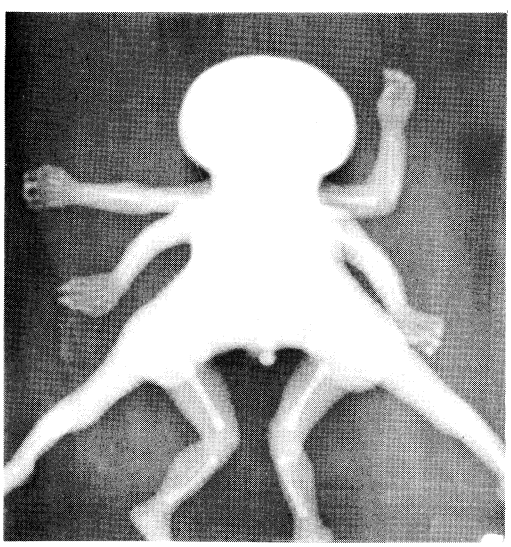

Fig. 3 Post mortem total body roentgenogram of conjoined cephalothoracopagus twins, anteroposterior view. Note the common head with two spines extension laterally, the fusion of the chest and abdomen and the four upper and lower extremities.

cord.

The total body roentgenogram confirmed the two separate spines (Figure 3).

Placenta

The placenta weighed 500 g. The placental plate appeared normal. There was one anmiotic sac.

The autopsy was not performed because of the mother's refusal.

The maternal postpartum course was unremarkable. Grief counseling was initiated. She was ready for discharge from the hospital on the third postpartum day.

Discussion

The exact incidence of conjoined twins is not known, but estimates of conjoined twinning have varied from 1 in 33000 to 1 in 165000 births[1-5]. An especially rare form is the cephalothoracopagus, with fused head and thorax. The actual incidence of cephalothoracopagus is vague. The malformation is said to occur in one of every three million births or one in 58 conjoined twins[6]. Data were analyzed on 228434 births delivered at Chulalongkorn Hospital over the period 1975-1989. The analysis identified 8 set of conjoined twins, for a crude incidence of 1 per 28500 births.

Stillbirths	2 cases(25%)
- Thoracopagus	1 case
- Cephalothoracopagus	1 case
Livebirths	6 cases(75%)
- Thoracoomphalopagus	2 cases
- Thoracopagus	1 case
- Ischiopagus tetrapus	1 case
- Dicephalus dipus triradius	1 case
- Dicephalus tripus tetrabrachius	1 case

Three types of cephalothoracopagus twins have been described[7]:

1. deradelphus : with one face and two ears

2. janiceps : with two faces on opposite side of the head

3. syncephalus : with a single face and four ears, two of which are on the back of the head.

This case appeared to be of the last variety. A review of the available English literatures shows that only a few cases of cephalothoracopagus syncephalus have been reported[4,5,8-16] (Table 1).

The most papers reported a single cortex, two brain stems, two thoracic cavities, two hearts, four lungs and a single gastrointestinal tract that bifurcated at the level of the small intestine. Most cases had two livers and normal genitourinary tracts. Some cases of triplet pregnancy associated with cephalothoracopagus have also been reported[16,17].

Mechanism of conjoining

Embryologically, conjoining results from a twinning event occuring between days 13 and 15 after fertilization[18]. The location of the connection and the degree and nature of organ duplication will depend on the area affected by the twinning event.

Conjoining, according to one theory, is the result of the incomplete separation of two embryonic axes in

Table 1 Caphalothoracopagus syncephalus : comparison of anatomical variations in reported cases (numbers indicate numbers of each organ present)

	Grundfast[5] 1950	Bartlett[8] 1959	Fahmy[9] 1966	Carlson[12] 1975	Furuhashi[13] 1980	Delprado[14] 1984	Benbridge[15] 1987
Central nervous system							
Cortex	-	2	-	1	1	3	1
Brain stem	2	2	-	2	2	2	2
Thorax							
Heart(s)	1	2	1	2	2	2	1
Connections	-	CA	-	CA	Heart to aorta	CA	-
Lungs	4	4	2	4	2	4	4
Gastrointestinal tract							
Esophagus	2→1	1	-	1	1	1	1
Stomach	1	1	1	1	1	1	1
Small intestine	1→2	1→2	-	1→2	1→2	1→2	1→2
Large intestine	2	2	2	2	1	2	
Pancreas	1	2	-	-	-	1	2
Liver	2	2	1	2	-	2	1
Genitourinary tract	NAD	NAD	-	NAD	NAD	1-NAD 1-H	NAD

H=Hydronephrotic, CA=Communicating artery, NIL=No connection, NAD=No abnormality detected

one ovum after the embryonic disc has formed[19]. On the basis of the mechanism of somite development, would duplicate themselves later than the more central areas. That theory is supported by the observation that conjoined twins are fused more frequently in the midaxial than proximal or distal areas. Sturrock and McKenzie[20] suggested a "collision" theory as the primary fault in the development of the cephalothoracopagus. The two cranial ends of the embryonic monozygotic twin axes lie close enough to meet or even fuse. The head regions and brain (or brains) are thus fused into one head, with various degrees of body fusion in a caudad direction. Such an explanation is attractive in terms of the findings in this case.

The prenatal diagnosis of conjoined twins is thus important for several reasons. It allows correct planning of the site and type of delivery, referral to a center where appropriate obstetric and pediatric surgical facilities are available[21,22]. The most important first step in making the diagnosis is awareness of its possibility. All sets of twins when examined with ultrasound should be shown to be separated from each other. If separation is suspected but cannot be confirmed, careful examination with realtime ultrasound allows full assessment of the site and type of conjoining, it being the method which shows the soft tissue conjunction. It also allows shared organs to be seen, and both babies can be carefully screened for other system

abnormalities. A number of sonographic and roentgenographic features of ventrally fused, conjoined twins have been described and listed (Table 2).

Table 2 Roentgenographic and sonographic features of ventrally fused conjoined twins[22-25]

Findings	Roentgenography	Ultrasonography
Fetal body parts on the same level	X	X
Constant relative fetal position	X	X
Fetal extremities in unusual proximity	X	X
En face fetal position	X	X
Bibreech, less commonly bicephalic presentation	X	X
Hyperextension of one or both cervical spines	X	X
Nonseparable, continuous external skin contour		X
Single heart sound by Doppler		X
Solitary large liver and heart		X
Multiple shared omenta		X
Solitary umbilical cord with > 3 vessels		X

Once the diagnosis of conjoined twins is established, the method of delivery should be based on the potential for infant survival, their size, type of joining, and parental attitudes[21].

When the diagnosis of conjoined twins is made before viability, the option of pregnancy termination should be offered to the parents. After viability, serial examinations are indicated to monitor fetal growth and the development of hydrops, and to detect fetal demise. The method of delivery depends upon the prenatal assessment of the likelihood of survival [26]. Although vaginal delivery is possible[27], dystocia occurs frequently[28]. Vaginal delivery should be reserved for stillbirth and for variety that are incompatible with life. A destructive procedure (embryotomy) can be considered for stillbirths. Caesarean section is the method of choice to maximize survival of the twins, because it decreases the risk of birth trauma and hypoxia. A vertical uterine incision is recommended. In cephalic / cephalic presentation, the heads should be delivered before the rest of the bodies. The same principle is applied to breech / breech and cephalic/ breech conjoined twins[26].

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SPECIAL ARTICLE

Faculty Perceptions of Ideal Teacher and Curriculum in Health Care Professions

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Abstract : *In curriculum development concept, the curriculum must be based on extensive assessment of both the need to be met (objectives) and the resources available to meet those needs. The successful facilitation of learning is dependent upon knowing the learner. The implication of this concepts is that a program of continuing professional education designed to improve curriculum development and instructional skill must begin by discovering the current concepts about curriculum and teaching. The objective of this paper is to answer whether the attitudes and beliefs of the health care professionals can be changed through continuing professional education.*

The instruments used is a Likert-type scale, consisting of 59 items, entitled "Status of medical and nursing school faculty and curriculum." The result of the perception is "yes" it can be change through continuing professional education. (Thai J Obstet Gynaecol 1990; 2: 43-58.)

Key words : ideal teacher, curriculum, health care professions

According to English and Kaufman[1], curriculum is means to and end; it is the "conscious and deliberate shaping of the major elements at the disposal of the educator to reach validated student objectives". As such, curriculum development (and the subsequent implementation of that curriculum) must be based on extensive assessment of both the needs to be met (objectives) and the resources available to meet those needs. Similarly, Roger[2] and Combs[3] state that the successful facilitation of learning is dependent upon knowing the learner.

One implication of above con cepts is that a program of continuing professional education designed to improve curriculum development and

instructional skills must begin by discovering the current concepts which the participants hold about curriculum and teaching. Thus, the Regional Training Center at Chulalongkorn University has sought to develop and utilize an instrument which would assess the perceptions of medical and nursing faculty to the ideal curriculum and teacher for the training of health care professionals. Today, we want to share with you the description of those two important aspects of professional training as they have been described by participants in the Academic Skills Courses held at the Regional Training Center in Bangkok.

The Department of Obstetrics and Gynaecology of the Faculty of Medicine at Chulalongkorn University has played a significant role in the development of reproductive health services in Thailand. Through its regional training activities it has been an important influence on key leaders in reproductive health services in Asia. The Johns Hopkins Program for International Education in Gynaecology and Obstetrics (JHPIEGO) has assisted the Department by sponsoring the development of serveral courses in reproductive health and the training of key personnel in reproductive health from Thailand and other parts of Asia. Aspects of these courses have been absorbed into the regular curriculum of the Department in its training of physicians (both clinicians and academicians). JHPIEGO courses have grown to become a useful vehicle for constant up-dating of Department courses while fostering on-going development of reproductive health services.

Instrument

The instrument used in assess participants perceptions was entitled "Status of Medical and Nursing School Faculty and Curriculum." It is a Likert-type scale, consisting of 59 items divided into two parts. The first 28 items address perceptions of the ideal teacher while the remaining 31 items assess concepts about the curriculum. The response scale is 1-5, with 1 = "Strongly disagree" and 5 = "Agree very strongly". Participants also have available a "No idea" option. The instrument was developed for the Regional Training Center with the cooperation of the Medical Education Unit, Faculty of Medicine at Chulalongkorn University.

Reliability of the instrument was determined through calculation of both Cronbach's Alpha and the Spearman-Brown Split-half coefficient. For the Ideal Teacher Scale, Alpha = .82 and the Spearman-Brown $\underline{r}$ was .71. For the Ideal Curriculum Scale, Alpha = .92 and $\underline{r}$ = .94. According to Balian, reliabilities in the 80's are "good" and coefficients in the 70's are "useful"; thus it was concluded that the instrument had sufficient reliability to yield useable data.

Sub-scale factors for both the Teacher and Curriculum Scales have been identified and checked for reliability. Reliabilities across the 5

Teacher factors and the 6 Curriculum factors were satisfactory for all factors (r's ranging from .67 to .91) except the Cost Effectiveness factor of curriculum (alpha = .48), which is a three-item scale.

Subjects

The data reported here were obtained from 45 participants in the first three Academic Skills courses held at the Regional Training Center at Chulalongkorn University. Approximately half of the participants (N=25) came from Southeast Asia, 8 from the islands of the Pacific Oceania, 8 from countries on or bordering the Indian Sub-continent, and 3 from the Near-east. Among them were 8 administrators or head teachers, 14 Professors or instructors, and 23 residents and staff members. One-third (N=15) were female and the remaining 30 were male. In terms of their institutions, 15 were affiliated with a University or College, 20 with a Teaching Hospital, and the remaining 10 participants were associated with a variety of Institutions, including government agencies (N=2), Nurse Training Institutions (N=4), and Maternal and Child Health Centers (N=4). All participants had responsibilities in the training of physicians, nurses, or midwives.

Because of these views, the curriculum should be relevant and flexible, should involve affective content, and should utilize enriched teaching methods. High standards of performance should be maintained but they should not be externally established. And, finally, cost effectiveness should be neither ignored nor bought at the expense of quality.

Results

Data reported here was obtained when the instrument was administered as a pre-test during the first day of the courses. In general, the participants agreed with the items proposed by the questionnaire for describing the Ideal Teacher and Ideal Curriculum. The grand mean across the 28 items for the Ideal Teacher scale was 3.54; for Ideal Curriculum, the mean of the 31 items was 3.17. Thus, the level of agreement for both sections of the instrument was between "Agree" and "Strongly agree"; although agreement with the teacher items was slightly more than one-third level higher than agreement with the curriculum items.

There was considerable variance among the individual items, with a median standard deviation of 1.04 for Curriculum Scale items and .92 for the Teacher Scale items. Agreement levels for sub-scale factors are reported below, separately for the two scales.

The Ideal Teacher

Analysis of the Ideal Teacher scale yielded five factors, each of which addressed a function which the teacher performs. These five factors and their interpretation are as follows:

Manage Instruction : These 6 items assess the degree to which the teacher is a manager of instruction.

Facilitate Students : These 9 items deal with interpersonal relationships in the learning environment.

Meet Individual Needs : These 6 items look at the degree to which the teacher is responsive to abilities and needs of individual students.

Transmit Medical Information : These 4 items assess the teacher's commitment to transmission of detailed medical information.

Maintain Control : These 7 items examine the teacher's control of students and the learning processes.

Table 1 presents the mean level of agreement and the standard deviation for each of the factors. As indicated, the participants agreed strongly that the ideal teacher should be a manager of instruction (X = 4.06) and a facilitator of students (X = 3.90). They were very consistent in their agreement upon these factors, with the median item standard deviations for the two factors being .69 and .78 respectively.

Figures 1 and 2 present the items in each of the first two factors and the levels of agreement with each item. The item with which everybody agreed most highly was that the ideal teacher would have self-confidence in teaching (See Fig. 1). Among the items in this factor, the participants were least sure (X=3.4) that the ideal teacher would spend time and energy in trying to be a leader in the academic field.

Table 1 Factors for the ideal teacher

Name of factors	No. of Items	Factors Mean	SD	Mean Item SD
Manage Instruction	6	4.06	.510	.69
Facilitate Students	9	3.90	.488	.78
Meet Individual Needs	6	3.56	.599	.97
Transmit Medical Information	4	3.44	.588	1.10
Maintain Control	7	2.76	.610	1.03
Total Ideal Teacher Scale	28	3.54		.92

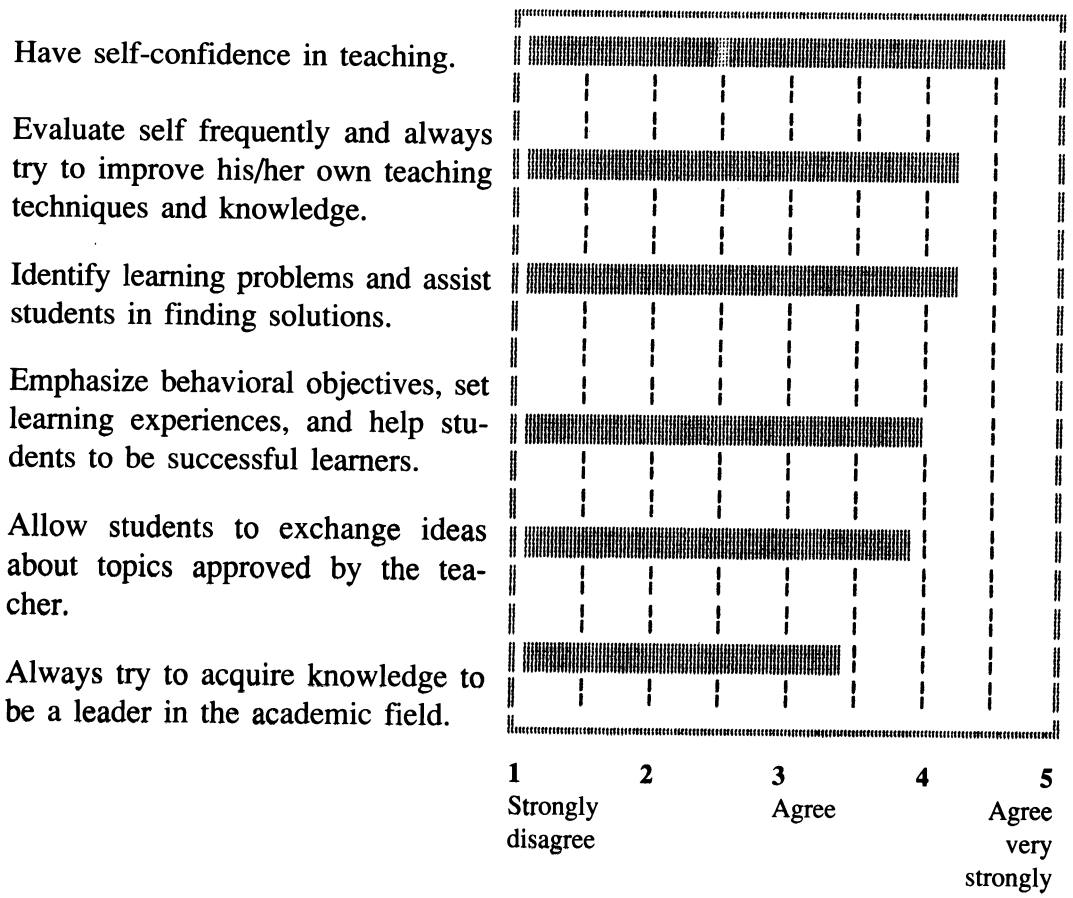

Fig. 1 Levels of agreement with items in the manage instruction factor

The participants agreed strongly with all but one of the items in the Facilitate Students factor. (See Fig. 2) They disagreed with the item suggesting that one way to facilitate student was by the instructor's modeling of life as a physician or nurse (X=2.5).

Be trustworth, so the students feel free to open their minds.

Provide students with opportunities to express freely their ideas and viewpoints.

Set learning experiences that allow students to learn by discussing and asking questions.

Maintain good conscientiousness and morality.

Emphasize behavioral objectives, set learning experiences, and help students to be successful learners.

Be reliable and available to students in need.

Create faith and respect among the students.

Create admiration for and positive valuing of medical professionalism.

Model life as a physician or nurse.

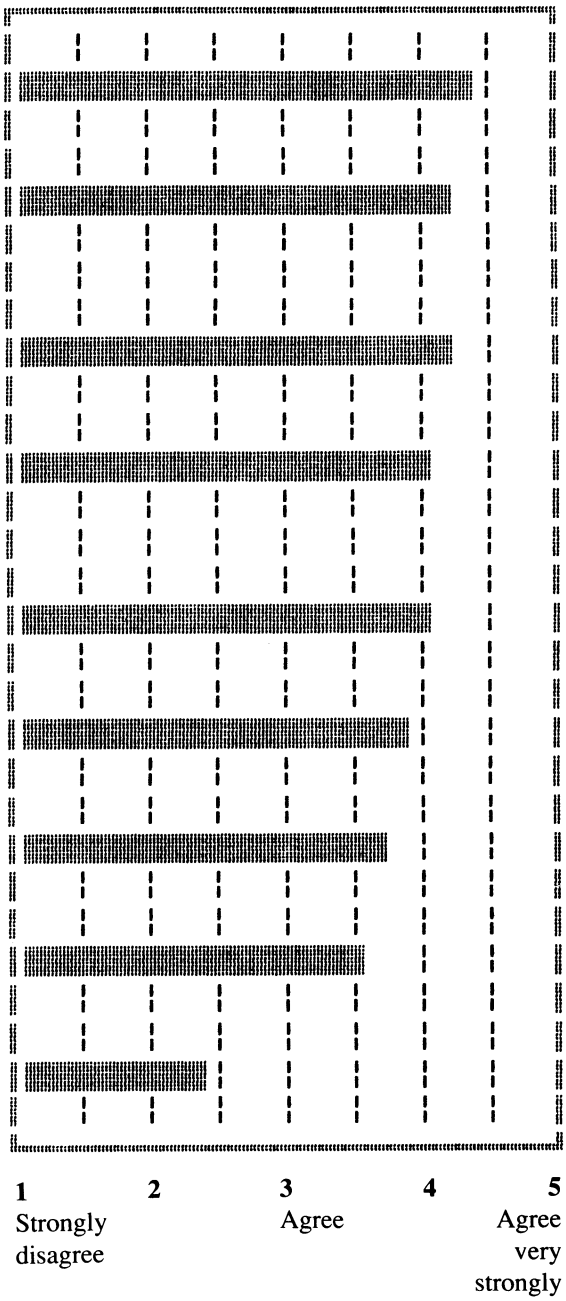

Fig. 2 Levels of agreement with items in the facilitate students factor

There were moderate levels of agreement for the teacher's functions in meeting individual needs (X=3.56) and in transmitting medical information (X=3.44). As indicated by the high median item standard deviation, however, the participants differed greatly as to their beliefs about the value of the items in the latter factor (Transmit Medical Information).

Figure 3 displays the items and agreement levels for the third factor. The participants indicated that doing research for an academic position (X=2.9) and putting a great deal of stress on the details of every subject (X=2.5) were not helpful in meeting student's needs. On the other hand, they felt that in ideal teacher would take the student's needs, abilities, and problems into account in planning programs and cooperative learning activities to make sure that students attained the expected learning outcomes.

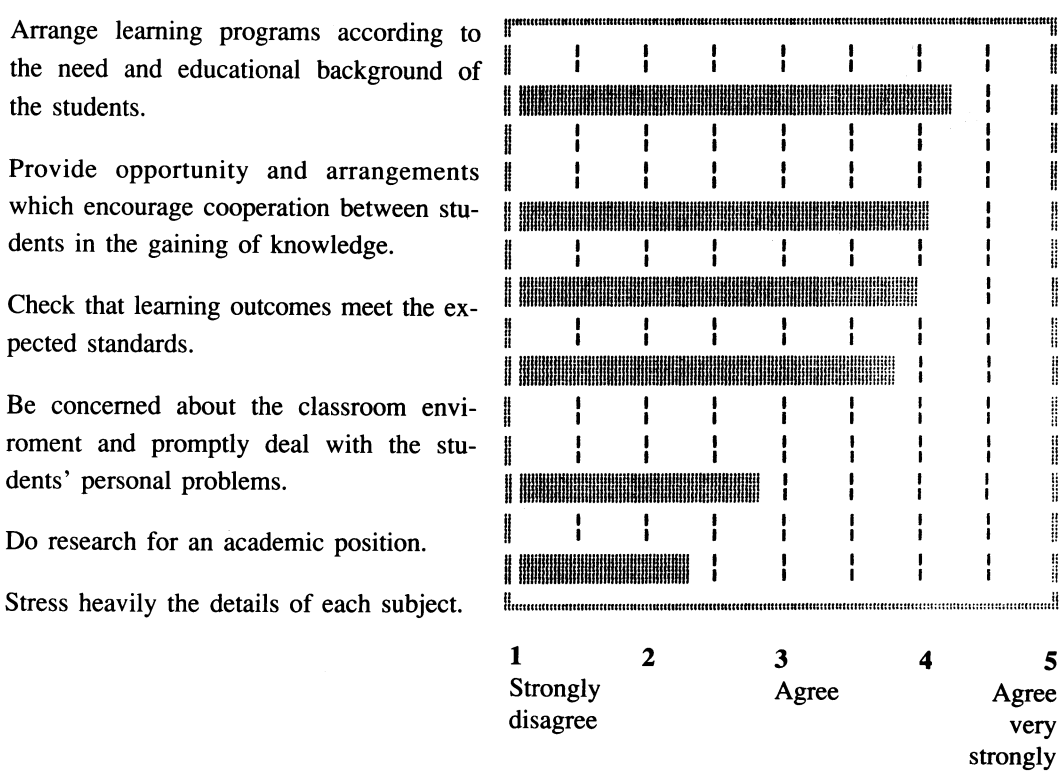

Fig. 3 Levels of agreement with items in the meet individual needs factor

As indicated by the data in Fig. 4, the participants felt that the ideal teacher would pass on medical knowledge on behalf of the physician and nurse by being a good role model, being conscientious, exhibiting morality, and providing students with opportunities to integrate knowledge by discussing the subjects. They did not agree, however, that the transmission of medical information would be accomplished by heavy stress on the details of each subject (X=2.5).

The final factor, Maintain Control, is comprised of a set of items with which the participants agreed only moderately or which failed to attain a mean level of "Agree". These items have rating means that range from 1.95 to 3.4, with only three of the four items reaching the 3.0 level.

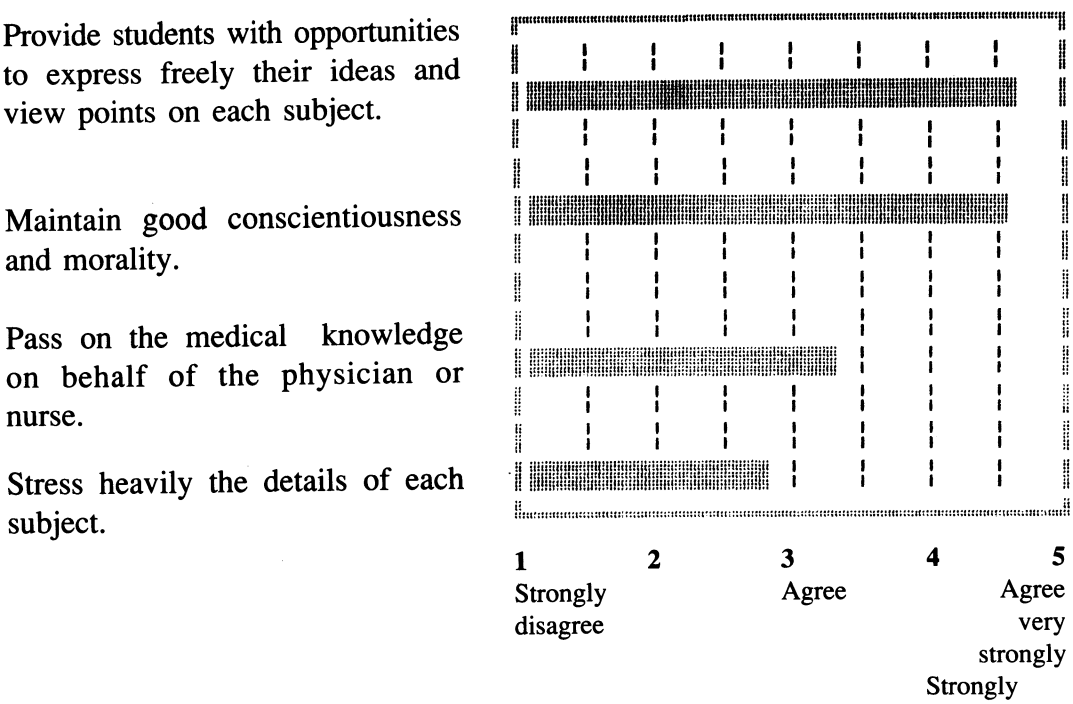

Fig. 4 Levels of agreement with items in the transmit medical information factor

Perform duty as assigned.

Plan educational strategy based on his/ her own concepts and skills.

Arrange learning processess according to the teacher's curriculum.

Train students to acquire the skills and capability of a specialist.

Frequently use a written exam. to test students' knowledge and ability.

Immediately correct a student's idea which is different from the teacher' s ideas.

Find ways of keep students from reacting to or objecting to the teacher's mistakes

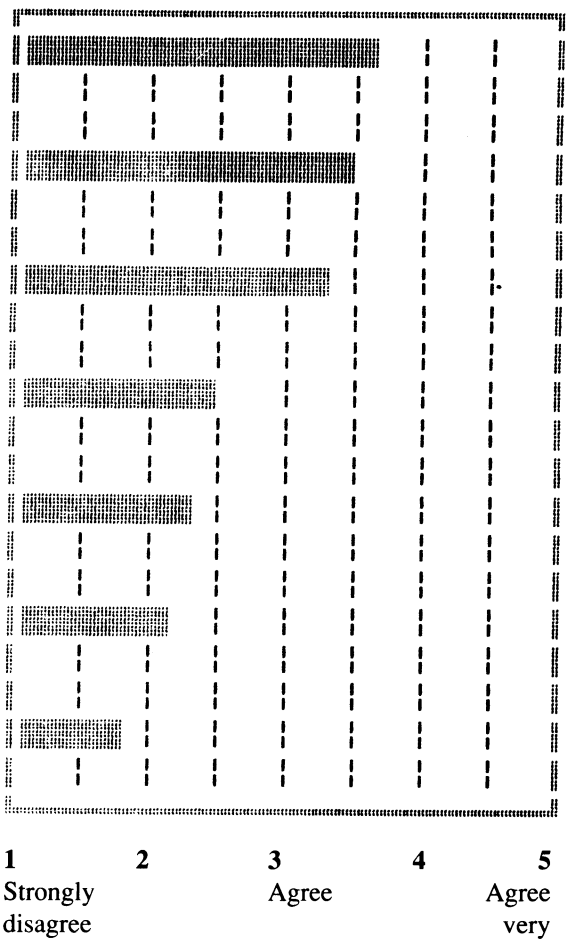

Fig. 5 Levels of agreement with items in the maintain control factor

In general, the participants indicate moderate agreement for the idea that the ideal teacher would be a conscientious teacher and take responsibility for arranging educational strategies and learning processes. How ever, the felt that the ideal teacher would not emphasize specialist training or the use of frequent written exam., nor would he/she be concerned with ensuring student agreement with the teacher's ideas. Finally, The ideal teacher would not worry about controlling student reactions to the teacher's mistakes.

In summary, the participants believed that the ideal teacher is one who manages instruction in a manner which encourages student interaction and integration of knowledge and critical thinking about medical information rather than just wrote memory of details. Furthermore, in planning and implementing learning activities, the ideal teacher would take into account individual needs, abilities, and interpersonal processes in learning and motivation. Finally, the ideal teacher

would rely on good planning and adequate learning activities to ensure learning; coercion and criticism were not seen as acceptable mechanisms for the control of student behavior.

The Ideal Curriculum

Analysis of the Ideal Curriculum Scale yielded six factors, each of which represented a potential characteristic of a curriculum.

The six factors and their interpretation are as follows:

Relevant : These 6 items address the degree to which the curriculum is responsive to individual and social contexts of education in the health care professions.

Flexible : These 6 items assess the ability of the curriculum to be adaptive to individual needs, new technology, and changing aspects of society.

Enriched : These three items assess the degree to which the curriculum encourages the enrichment of instruction through use of Audio-Visual aids and new teaching technologies.

Affective : These 4 items address the affective aspects of the curriculum.

Cost Effective : These 3 items address the trade-off in the curriculum between costs and quality.

Standardized : These 9 items address the way the curriculum handles the establishment and maintenance of standards.

Table 2 presents the mean level of agreement and standard deviation of each of the above factors. As indicated in the table, the participants agreed very strongly that a curriculum should be relevant and flexible (X's of 3.61 and 3.60, respectively). They also felt that the curriculum should be enriched (X=3.30) and should deal with affective goals and concerns of students (X=3.27). They were less concerned with cost effectiveness (X=2.71) and standardization (X=2.64).

Table 2 Factors for the Ideal Curriculum

Name of factors	No. of Items	Factors Mean	SD	Mean Item SD
Relevant	6	3.61	.82	.96
Flexible	6	3.60	.82	1.01
Supplemented enriched	3	3.30	.76	.98
Affective	4	3.27	.90	1.07
Cost effective	3	2.71	.94	1.09
Standardized	9	2.64	.77	1.12
Total Ideal Curriculum	31	3.17		1.04

Figure 6 displays levels of agreement for the items in the Relevent Factor. The first five items were strongly supported by the participants as being ways in which the ideal curriculum would be relevant for students. The ratings of the last item, with which the participants disagreed, affirms the need to be able to adjust the curriculum so that it can be relevant.

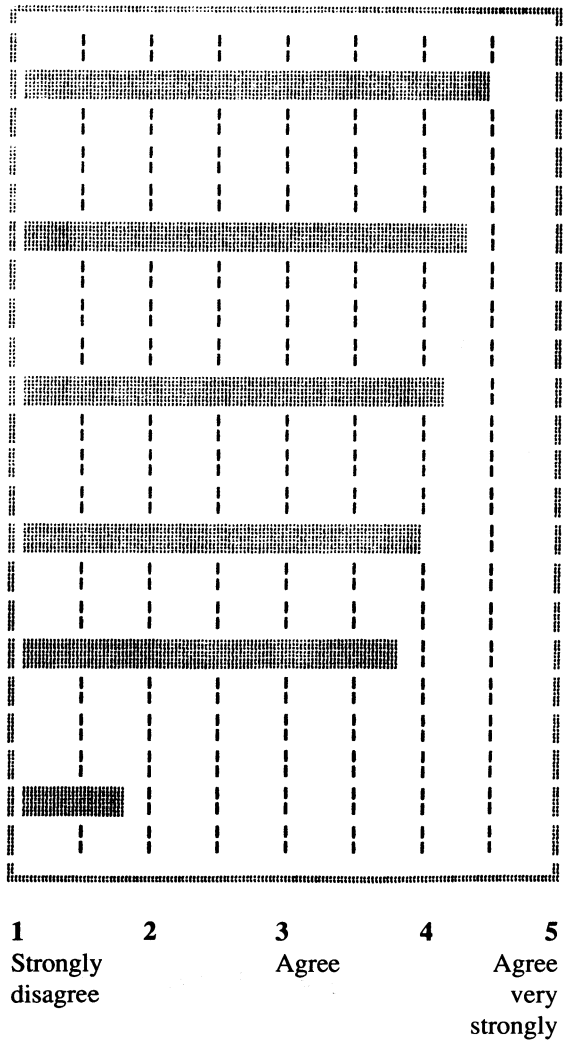

Fig. 6 Levels of agreement with items in the relevant factor

The flexible is similar in directionality to the relevant factor, however, it is more concerned with emerging processes in the curriculum rather than the relationship of the curriculum to its context. All items in the factor except one attained the "Agree" level. (See Fig.7).

Produces medical school graduates according to Health Needs.

Attempts to solve health problems by carefully studying social problems.

Adds new academic knowledge from new technology.

Arrange contents sequentially in relation to the educational level.

Provides for students to learn by practicing.

Sets social values and desired behavioral changes according to the mental development of students.

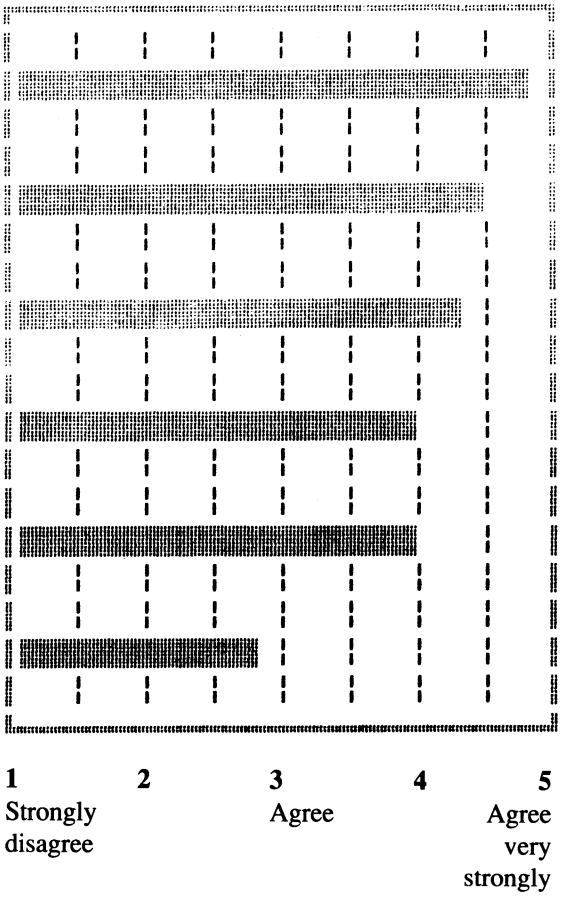

Fig. 7 Levels of agreement with items in the flexible factor

As indicated by the levels of agreement in Fig.8, the participants felt strongly that a good curriculum would encourage the enrichment of instruction through the use of audio-visual aids and new teaching technologies.

There was considerable variance among the participants in their responses to the items in the Affective Factor (the median standard deviation for the items was 1.07 which is equivalent to one level), however, they did affirm the importance of this characteristic of the curriculum at a moderate level of agreement. The only item in the factor which fell below the 3.0 mean rating was the item regarding the extra expense of multidisciplinary learning (See Fig.9).

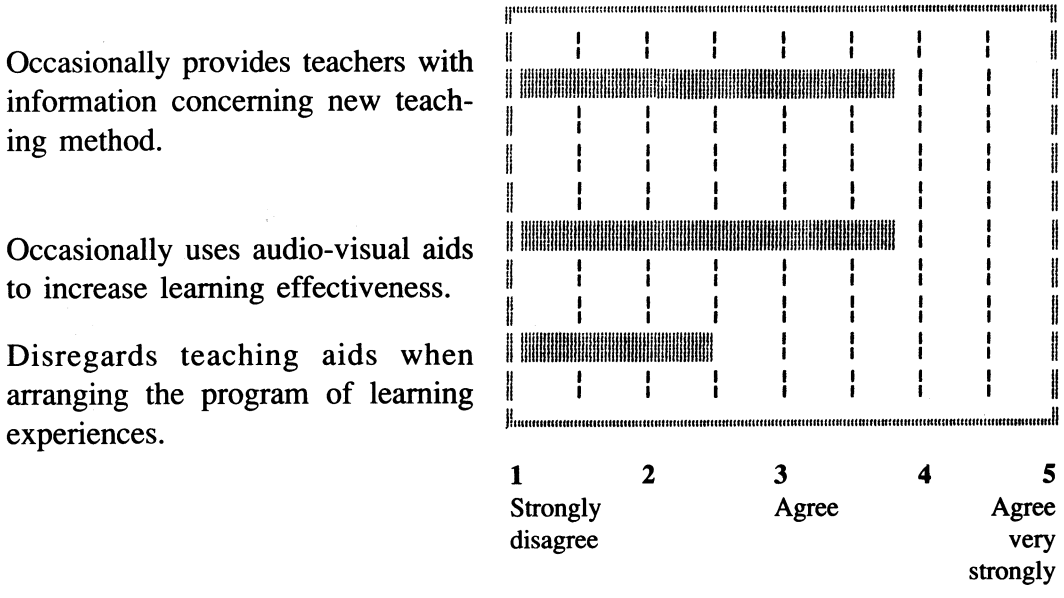

Fig. 8 Levels of agreement with items in the enriched factor

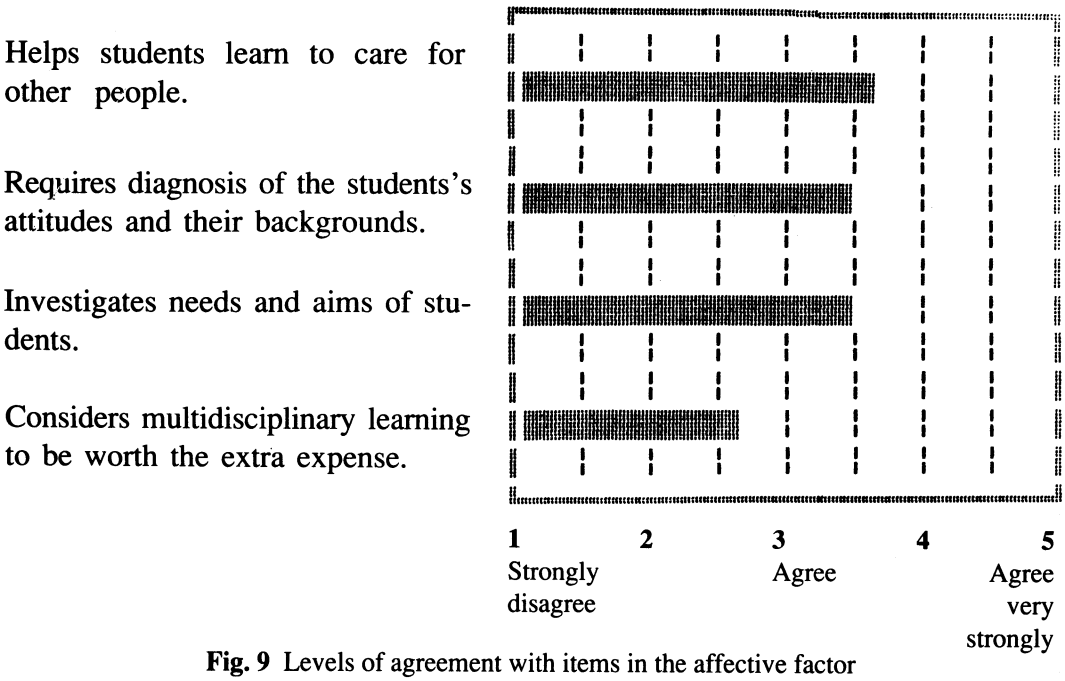

Fig. 9 Levels of agreement with items in the affective factor

As indicated in Fig.10, the participants fully disagreed with the idea that the curriculum should disregard cost effectiveness while producting medical graduates. They supported a curriculum which was not over-lapping or redundant and they felt that overemphasis on the details of subject matter was not cost-effective.

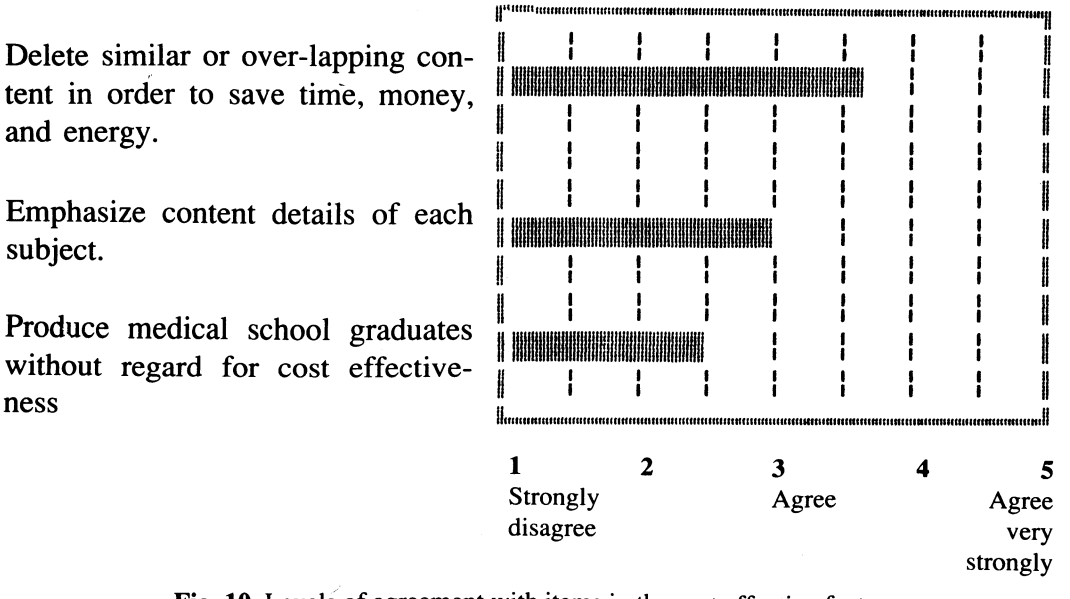

Fig. 10 Levels of agreement with items in the cost effective factor

The final factor dealt with the degree to which the curriculum is standardized. As shown in Fig.11, the participants felt that learning experiences should be provided according to the resources available to the teacher and student and that the basic knowledge and learning ability of the students should be more than a manor factor in curriculum decisions. They further indicated that externally-established standards were not compatible with the goals.

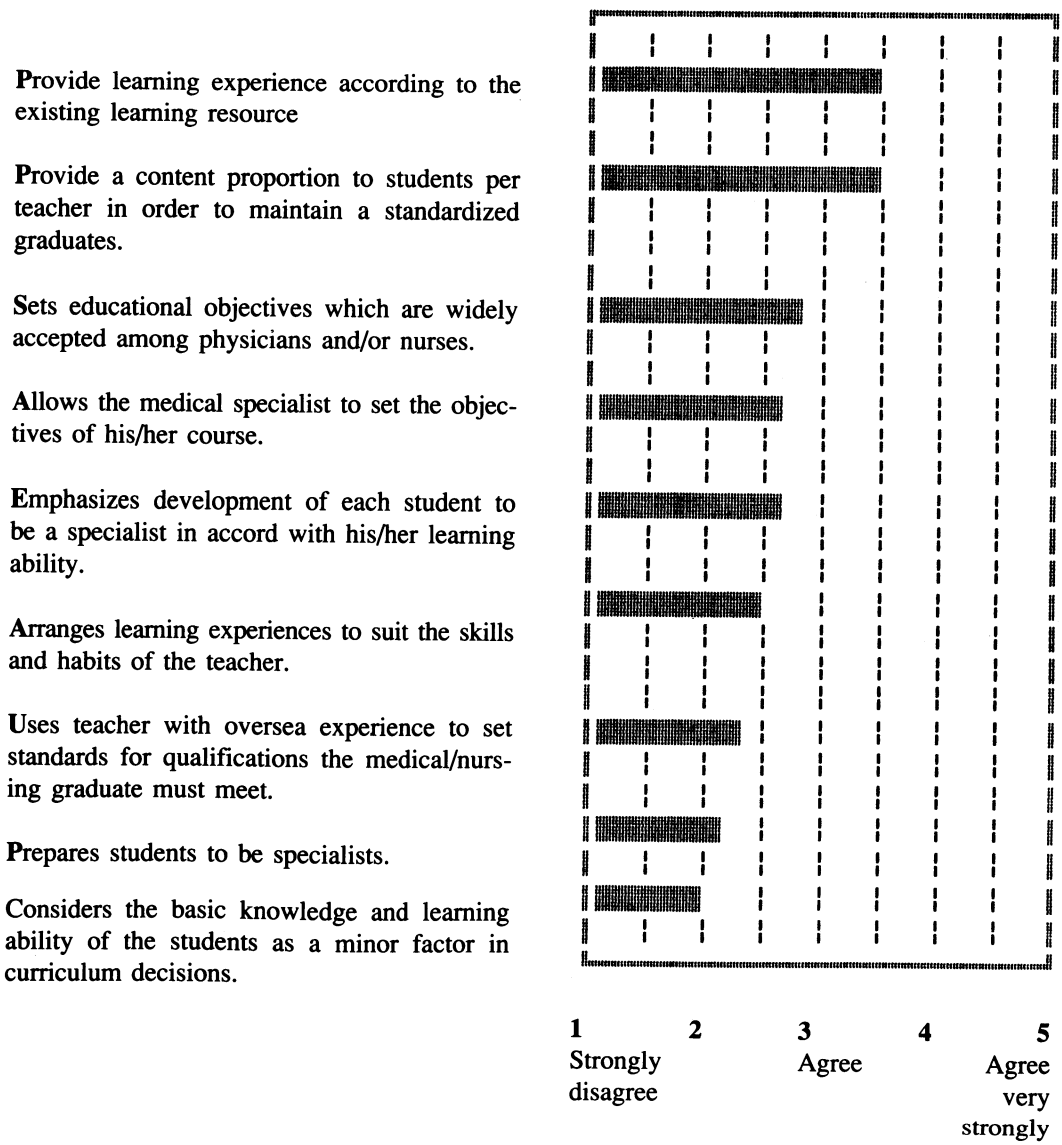

Fig. 11 Levels of agreement with items in the Standardized Factor

In summary, the participants view curriculum as a means to an end. And that end...that goal...is seen as a medical graduate who is caring of others, who is prepared and willing to address the Health Needs of the nation,who can cope with the environment and varying local situations and can engage in life-long learning.

Conclusion

Having described the attitudes and beliefs of the participants who are involved in the preparation of physicians and nurses regarding the ideal teacher and curriculum, the question naturally arises : Can these attitudes be changed through continuing professional education? This question was addressed by the Regional Training Center (and reported elsewhere) and the answer is "Yes". In the three-week course in Academic Skills, conducted by the Regional Training Center at Chulalongkorn University, significant pre- to post- training movement occurred in five of the 11 factors.

Furthermore, trends closely approximating significance occurred in two other factors. Significant movement occurred in the Ideal Teached factors of Facilitate Students and Meet Individual Needs and in three of the Ideal Curriculum factors: Standardized, Affective, and Cost Effective. In all cases, the movement was in the direction of the instruction which had been conducted during the workshop.

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