中華民國周產期醫學會
1995 年度報告

臺灣之多胞胎姙娠

Taiwan Society of Perinatology
1995 Annual Report

Multifetal Pregnancy in Taiwan

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Foreword

Taiwan launched its general health insurance in March 1995. The adequate prenatal care of pregnant women, annual physical checkup for children, and vaccination of children received emphasis as a measure of preventive medicine. This promises Taiwan to have a healthy generation for the 21st century. Preventive medicine consumes lots of manpower and resources to prevent the consequence and burden of disease. How to properly care for the health of the mother and baby is the main goal that Taiwan Society of Perinatology is trying hard to reach.

Preceded by the reports on "The congenital malformation: background, prenatal diagnosis, postnatal management in Taiwan" and "Prenatal care for the 21st century", this coming annual report of 1995 focuses on the topic of "multifetal pregnancy".

As we know, multifetal pregnancy involves the issues of race, genetics, and the application of reproductive technology. The prenatal care of multifetal pregnancy should be managed as high risk pregnancy. How to prevent the complication and the occurrence of prematurity are the main issues. Multifetal pregnancy is usually complicated by low birth weight and prematurity. The more proper neonatal care provided by the neonatologist, the higher survival rate and the lower morbidity of the newborns could have. There is also a big challenge to parents raising the babies of multifetal pregnancy.

In Taiwan, we have held international symposia to discuss the issue of twin pregnancy, but we still need to conduct more research on the occurrence and the prenatal care of multifetal pregnancy to collect a sizable domestic data base .

This annual report is the brainchild of Dr. Ming-Kwang Shyu. Also Professor Fon-Jou Hsieh, Dr. Hei-Jen Jou, Dr. Ru-Jeng Teng, Chuo-Hsiung Yen, and Ms. Ming-Chih Wu contributed their efforts in the preparation of this very important document.

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T'sang-T'ang Hsieh
President,
Taiwan Society of Perinatology
December 1995

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前　言

　　台灣從1995年3月開辦全民健保，其中預防保健項目中的孕婦產前檢查及孩童健康檢查與預防注射為首要之推展目標，以期能有健康傑出的下一代迎向21世紀。預防保健是事前的人力，心力及財力的投資以避免事後更多的煎熬與負擔。如何做好婦幼保健的工作是周產期醫學會努力自許的任務。

　　繼“台灣先天性畸型之現狀”及“台灣之產前檢查—展望21世紀”之後，周產期醫學會1995年的年度報告題目為“多胞胎”。多胞胎妊娠涉及種族，遺傳和生殖科技的應用。多胞胎妊娠的周產期罹病率與死亡率遠高於單胞胎妊娠，母親懷孕時的併發症亦高於單胞胎妊娠。多胞胎妊娠的產前照顧又考驗著對高危險妊娠處理的醫療水準，如何追蹤胎兒成長與健康，如何選擇生產方式，如何預防併發症及早產的發生是主要課題。多胞胎常有體重不足及不成熟兒的誕生，完善的新生兒照顧，提高存活率與降低罹病率是新生兒專家接下來的棒子，之後父母對多胞胎的養育及教育也是一大挑戰。

　　國內曾舉辦雙胞胎的國際大型集會，除了欣賞金銀婆婆的風采之外，我們更需要對多胞胎兒的發生，產檢與照顧的完整研究，為本土的婦幼衛生留下資料。感謝此次年度報告由徐明洸醫師負責統籌，謝豐舟教授、周輝政醫師、滕儒錚醫師及顏兆熊醫師、吳敏智小姐等組成工作小組，費心地完成此項任務。

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中華民國周產期醫學會
理事長　謝　燦　堂
1995年12月

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Preface

Multifetal pregnancy is a fascinating yet puzzling phenomenon in human reproduction. It's really amazing looking at the two phenotypically, almost the same individuals. The scenario of a conjoined twins was especially astunding. For long time twin study has been playing an important role in genetic study to differentiate genetic component from evniromental component of a certain trait. In the field of perinatal medicine, multifetal pregnancy poses an enormous challenge to the caretakers since multifetal pregnancy was clearly associated with increased perinatal mortality and morbidity arising from increased prematurity and a whole spectrum of fetal disorders, for example, twin-twin transfusion syndrome.

Recently the issue of multifetal pregnancy gathers more and more attention thanks to the popularity of assisted reproduction technology(ART) and the aging of pregnant women. Nowadays ART accounts for at least 25% of multifetal pregnancies.

Following the tradition of producing an annual report to address a specific issue in maternal-child health of Taiwan, Taiwan Society of Perinatology chose "Multifetal Pregnancy in Taiwan" as the topic of its 1995 annual report. In this report, all the relevant information in Taiwan concerning multifetal pregnancy were deliberately collected and tailored to convey a panorama of multifetal pregnancy in this Island Nation.

Not only medical aspects of multifetal pregnancy were presented, genetic aspects and developmental aspects were also included. With this background data, we hope to stimulate future research of multifetal pregnancy in Taiwan and better perinatal care can be rendered to the multifetal pregnancies and their mothers. Moreover we prepare to load the content of this annual report on the Internet. Thus exchanging information concerning multifetal pregnancy with the whole world can be achieved.

Finally, may God bestow good health and happiness on the existing and upcoming twins, triplets, quadruplet.......

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序　言

　　多胞胎妊娠是人類生育中既有趣又令人迷惑的現象，兩個幾乎一模一樣的雙胞胎實在是越看越有趣，而連體嬰更是令人難忘的視覺經驗。長久以來，雙胞胎研究一直是遺傳研究中區分遺傳因素與環境因素的有力工具，在周產醫學的領域中，多胞胎妊娠對醫療人員更是一項鉅大的挑戰。這是因為多胞胎的周產期罹病率與死亡率都較單胞胎顯著提高。當然這是由於多胞胎的早產率較高，尚且還有種種的胎兒問題，例如雙胞胎輸血症候群..............等等。

　　近來多胞胎的問題愈發受到重視，這是因為人工生殖科技的廣泛使用以及產婦年齡的升高增加了多胞胎的發生率，例如目前多胞胎至少有百分之二十五的是人工生殖科技的產品。

　　依循本會每年針對台灣當前婦幼衛生課題，製作年度白皮書的傳統，台灣周產期醫學會今年選擇了"台灣之多胞胎妊娠"作為 1995 年的白皮書主題。這本白皮書中包含了我們所能搜尋到的有關台灣多胎妊娠的所有資料，經過細心的整理，以使讀者能一窺台灣多胞胎妊娠的全貌。

　　這本白皮書不僅包含了多胞胎在醫療上的資料，有關遺傳學及發育學的資料也包羅在內。藉由這些資料的彙集希望能刺激台灣將來的多胞胎研究，並使我們對多胞胎及其母體提供更好的周產期照護。在這"網際網路"風行的年代我們也準備將這本白皮書的內容置於網路之上，使台灣有關多胞胎妊娠的資訊能與世界各國互相流通。

謝　豐　舟　　教　授
台 大 周 產 醫 學 中 心
1995 年 12 月

Multifetal Pregnancy in Taiwan

Introduction

Fertility has a special place in almost all cultures. The ability that a woman can bear children is 'critical in the development of a sense of femininity, gender identity, and self-esteem...'. Just as infertility may be a threat to a woman's self-esteem and identity, 'excess fertility', as occurs in multifetal pregnancies, may be just as threatening.

As we know, multiple gestations bear higher perinatal mortality and morbidity than singletons, but actually, limited data could be collected about the incidence of multifetal pregnancy, their epidemiology, the mortality and morbidity in Taiwan. On this purpose, we review the domestic data available in the literature and also present some recent studies in this field.

Assisted reproductive technology (ART) has made a great impact on the ecology of the twins and other multifetal pregnancies in recent years due to the rapid growth of the infertility practitioners and laboratories. The grand multifetal gestation produced by ART warrants the fetal reduction to reduce the risk of extreme prematurity. We make some discussion about the issue of fetal reduction in multifetal pregnancies and direction for furthter research.

Lastly, we talk about 'twin-twin transfusion syndrome', which results in high perinatal mortality and morbidity in the twin. The mechanism and clinical pictures are presented. Our recent data has shown active management could be effective in some way, but further effort in correcting the underlying pathologic process are necessary in the future.

Epidemiology

The multiple pregnancy rates increased in recent years. If reviewed from the 1950s, the rates decreased gradually from the late 1950s to 1973, slightly increased and remained stable from 1974 to 1980, and then increased strikingly from 1981 to 1990. (Chen CJ, 1992b) (Fig. 1 &2)

The twinning rate in the four study hospitals in Taipei city between October 1985 and June 1989 was 11.5 per 1,000 deliveries (844/73,264). Based on Weinberg's rule(the number of Dizygotic pairs was twice that of different-sexed twin pairs), monozygotic (MZ) and dizygotic(DZ) rates were estimated as 7.5 and 4.0 per 1,000 deliveries, respectively.

In recent 5 years, the twinning rate showed further increase. At NTUH, between January 1991 and April 1995, the twin rate was 2.15%(243/11309) and if excluded twins by ART, 1.41%(158/11224). Similar trend was also seen at Chang-Gung Memorial Hospital between July 1990 and October 1995, with 1.48%(364/24648) and 1.26% (309/24593), respectively. If the result from Mackay Memorial Hospital was included, the recent overall incidence of twin pregnancy at Taipei was 1.55%. (table.1,2,3) Excluding twins produced from ART, the natural occurence rate of twins was 1.30%.

The overall triplet rate was 0.14%. Excluding triplets produced from ART, the incidence was 0.019%. The quadruplet rate

was 0.015%, all were from ART pregnancies.

Zygosity Few studies discussed about zygosity of the twin. The zygosity was usually determined by sex, placentation and RBC antigens. Unlike to the situation on the United States, where one third of all twins were monozygotic, the percentage of monozygoticy was higher in Taiwan. Either by Weinberg's rule or data calculation, the percentage of MZ varied from 56%(Teng RJ,1994), 60%(CGMH) to 66%(Chen CJ, 1992b). Recent data at NTUH showed that assisted reproductive technology(ART) markedly influenced the dizygotic rate within the twins. The percentage of dizygotic twin in NTUH in recent 5 years was about 51% for all twins (with 30.7% of these twins conceived by ART), and about 28% excluding twins conceived by ART. (table.2) If we arbitrarily set the percentage of ART of the twin to about 15%, which very near to the percentage of the twins by ART from the data at the CGMH in recent 5 years, the dizygotic rate would be 39%, which meant monozygotic rate to be 61%, very similar to the results of the others.

Parity and Maternal age The twin rate increased with parity and decreased with maternal age.(Tab.4) The odds ratios for both MZ and DZ twinning were found to increase with parity and decrease with maternal age. There was no significant difference in paternal age between the twins and singletons.

Assisted reproductive technology(ART) ART accounts for a significant proprotion of multifetal pregnancies in recent years. The percentage of twins by ART in all twins was 15.1%(55/364) at CGMH and 30.7% (70/228) at NTUH. All the triplets at NTUH(19/19) and 61%(11/18) at CGMH were produced by ART. (table.3)

Male to female ratio The ratio of males to females was 1.03 (671/651) (Hsieh TT,1992) in twins compared to 1.08 in singletons (Hsieh TT,1991). Even lower male to female ratio (0.93) was reported by Teng (352/380). (table.5) In natural pregnancies, there is a tendency that the percentage of male conceptions decreases as the number of fetuese in utero increases (table.6). A possible explanation is that the female-producing zygote has a greater tendency to divide. On the other hand, the male proportion in the DZ twins is higher than the MZ twins (table. 7) .

Higher male proportion can be seen in the pregnancies made by ART. The male to female ratio in triplets conceived by ART is 1.32 (NTUH) and 1.20 (CGMH), respectively(table. 8). The male to female ratio in twins from ART is about 1.12 at NTUH and 1.19 at CGMH, respectively, still higher than that in singletons and overall twin pregnancies. It is reasonable to propose that male proportion can be raised during ART manipulation. However, one interesting thing is that lowest male to female ratio (0.84) is seen in the pregnancies from *in vitro fertilization* (IVF) amongst the various forms of ART, which may implicate the possibility of adverse effect of *in vitro* microenvironment to male-producing zygote. (Table. 9)

Perinatal Mortality and Morbidity

Preterm delivery The multifetal pregnancies had higher rate of preterm deliveries, which occurred before 37 complete weeks of gestation. The frequency of preterm births was 75% and 36.9%, respectively, for triplets and twins, compared to 5.6% for singletons.(NTUH; CGMH ; Hsieh TT, 1991 & 1992) Similar results were shown by Teng

RJ, in 1994. The frequency of low birth weight (<2500 g) for triplet, twin and singleton was 79.6%, 47.9% and 5.9%, respectively. The average period of gestation was about 39.2, 36.5 and 32.6, respectively, for singleton, twin and triplets. (Table. 10)

RDS Respiratory distress syndrome (RDS) was the most common neonatal morbidity in twins due to preterm births and low birth weights. The reported incidence of RDS was about 8% for the twins. (Ho SK, 1975; Lai PC, 1994). Almost all cases were seen in those born before 36 complete weeks and with lower birth weight(<2000g). The second twins were more frequently affected by RDS than the first twins. Most of the neonatal morbidities are related to RDS such as intraventricular hemorrhage, chronic lung disease, and retinopathy of prematurity. In triplets, the incidence of RDS was even higher (20.0%).

Mortality The neonatal mortality rate in twins varied from 18 per 1,000 live births (Hsieh TT, 1994) to 47 per 1,000 live births(Lai PC, 1994). Most of these cases were born before 32 complete weeks of gestation and with very low birth weight(<1,500 g). The perinatal mortality was 54 and 121 per 1,000 deliveries, respectively, for twins and triplets(Chen CJ,1992a;NTUH+CGMH, 1995).(Table. 10)

<u>Zygosity</u> The zygosity of the twins did infuenced the perinatal mortality rate. A study at Taipei city (Chen CJ, 1992a) showed that the perinatal mortality rates were 7.5%,1.4% and 0.7%, respectively, for MZ twins, DZ twins and singletons. Compared with singletons, MZ and DZ twins had a much higher perinatal mortality rate with a relative risk factor of 10.0 and 1.9, respectively. (Chen CJ, 1992a) The concordance rate of perinatal death(i.e. the rate of the perinatal death of the cotwin when one twin fetus died in utero)was 60% and 0%, respectively, for MZ and DZ twins. The monozygotic twins had higher chances of monochorionicity and, therefore, higher chances of intraplacental vascular communications which resulting in twin-twin transfusion syndromes (TTTS) or other obstetric complications. It could partially explain the higher perinatal mortality rate and concordant cotwin death in the MZ twins.

Section rate The cesarean section rate was high in the twins. It was 44.2%, 77.2% and 92.9%, respectively, for the years of 1983-1985, 1989-1991 and 1990-1995. (Lai PC,1994;CGMH,1995) The increasing rate may reflect the present attitude of the obstetricians in managing twin pregnancies. Although higher incidence of prematurity could be closely associated with the higher mortality rate in twin pregnancy, the mode of delivery might have some contributions. In Lai's series, when the gestational age was between 27 and 31 weeks or the birth weight between 1,000 and 1,499 g, vaginal delivery would have a higher mortality rate, especially for the second twin.

Twin sequence and morbidity In 1971, Ware had found a trend toward low 1 minute Apgar score among second twins delivered by version and extraction. In 1988, Ghai and Vidyasagar also claimed that the second twins had a higher rate of low Apgar scores even at 5 minutes.In one study(Lai PC,1994), higher incidence of hyaline membrane disease(HMD) and neonatal death was noted for the second twins, especially when the gestational age below 32 weeks or the birth weight below 1,500 g. In Lai's series, vaginal deliveries resulted in significantly higher morbidity and mortality than cesarean section deliveries. Cesarean section was therefore recommended for the deliveries if gestational age was less than 32 weeks or the expected birth weight was less than 1,500 g.

Congenital Malformations

Prevalence   The prevalence of major congenital malformations in twins was higher than singletons.The major congenital malformations included anencephaly, hydrocephaly, meningocele, cleft lip, cleft palate, cleft lip with cleft palate, congenital heart disease, imperforated anus, hypospadia, club foot, distal limb anomalies, chromosome abnormalities, acardiac monster, conjoined twins and others. In recent 5 years at NTUH, the congenital malformation rate was 2.1% for the twins, higher than the previous report for singletons(1.13%; Shyu MK, 1992). It was 1.5% for the twins at CGMH, in recent 5 years. In a more strict way of study(Chen CJ, 1992a), the incidence of major congenital malformations of the twins was 2.1%, which was about four times of the control-singletons(0.6%). The MZ twins also had a much higher prevalence of major congenital malformations (2.7%) than the DZ twins (1.0%), giving a relative risk factor of 4.6 and 1.7, respectively, comparing with the singletons. These results, consistent with many previous studies, suggest the adverse effects of the intrauterine environment in twin pregnancies on the development of congenital malformations.

Concordance rate   Chen's series also showed that MZ twins had a higher concordance rate for major congenital malformations (18%) than DZ twins (0%). The concordance rate of the facial clefts was 29% for MZ twins,which was lower than the previous studies at others countries. The low concordance rate of facial clefts among MZ twins (not 100%)suggested that the intrauterine environment in the development of facial cleft might play a relatively more important role rather than the genetic involvement.

Conjoined twins   Conjoined twins are considered the most tragic malformations of MZ twins, which result from the imperfect division of the embryo after the formation of two embryonic discs. The prevalence rate of the conjoined twins varies greatly from one country to another. In the study of Taiwanese of Taipei city, the prevalence rate was 2.7 per 100,000 deliveries. But it was ten times higher at NTUH in recent 5 years (26.5 per 100,000), which may be due to higher referral rate.

In 1979, a set of ischiopagus was born in Taichung who were subsequently surgically seperated. However both of the twins suffered from major handicaps. In 1981, Chen, Hsieh and Huang reported the first prenatal diagnsos of an omphalopagus at 28 weeks of gestation. The omphalopagus was delivered at 35 weeks and successful separation was achieved resulting in two healthy infants. In the 1980s, another 4 sets of conjoined twins were diagnosed prenatally, all at the third trimester. All 4 sets did not receive surgery because of significant cardiac or brain conjoining. In the 1990s, prenatal diagnosis of conjoined twin were also reported sporadically. In contrast to 1980s', the conjoined twins in the 90s' were usually detected at early second trimester and termination of pregnancy were usually persued.

Intrauterine Growth and Growth Discordancy

Birth weight   It is well-known that the growth of a twin fetus is slower than a singleton fetus. The mean birth weight (BW) of twins was quite similar to that of singletons before the 33rd week of gestation, but the

mean BW dropped to below the 10th percentile of that of singletons after the 37th week of gestation (Teng RJ,1994). The study of the CGMH, with 661 sets of twins enrolled (Hsieh TT, 1992), showed that the twin fetus grew most rapidly from the 32nd to the 35th week of gestation (200 g per week). The growth was 145 g per week from the 28th to the 32nd week and from the 35th to the 38th week of gestation. After the 38th week, the mean BW increased by only 35 g per week. Compared with a singleton birth, the mean BW of the twins was about 100 g lighter during the 28th to 32nd week, then the difference increased gradually to about 500 g at term. (Hsieh TT, 1992)

Sequence of the twin and fetal weight Two series in Taiwan had shown that the mean BW of the the first twins was greater than that of the second twins(2,459 ±537 g vs 2,404 ±548; Hsieh TT, 1992). Second twins had a greater frequency of low BW (< 2,500 g)than first twins (50.5% vs 45.2%). However, second twins were not significantly smaller than corresponding first twins of the same gestational age. The mean BW discordance was similar in two groups, i.e. 11±10% (Hsieh TT, 1992) and 10.4±9.0% (Lai PC, 1994) (intertwin BW difference / BW of larger twin), respectively.

Fetal sex and birth weight The mean birth weight of male twins (2,476±527 g) was greater than that of female twins (2,386 ± 555 g), and female twins had a greater frequency of low birth weight than male twins. (Hsieh TT, 1992)

Growth discordancy and neonatal adverse events As mentioned above, unequal intrauterine growth is not infrequently seen in twin pregnancies. The mean discordance was around 10.4±9.0% to 11±10%, with first twins heavier than second ones. One study about discordant twins (15% or more birth weight difference) showed a tendency for adverse events to occur in discordant twins, especially in the smaller cotwin. (Hsieh TT, 1994) A smaller twin weighing no more than 2,000 g has a 10 times greater risk to develop an adverse event as compared to a twin with a birth weight over 2,000 g and a similar gestational age; while a twin with a gestational age of less than 34 weeks has a 5 times greater risk than one 34 weeks or over with a similar birth weight. Through logistic regression analysis, it was found that birth weight and gestational age, but not discordancy, were the predictors of the occurrence of adverse events.

Fetal Reduction in Multifetal Pregnancy

With the advances of assisted-reproductive technology (ART), the incidence of multiple pregnancy increased markedly. The average gestational weeks at delivery were about 37, 33 and 31 weeks, respectively in twins, triplets and quadruplets from previous literatures, which showed the higher the order of fetal multiplicity, the shorter the period of conception. The prognosis of pregnancies with triplet or quadruplet was worsened by premature delivery and other complications, which became a major challenge for the obstetrician.

Fetal reduction In 1985, Lopes et al first reported the technique of selective termination in grand multiple pregnancy. However, the procedure was usually complicated with rupture of membrane, abortion, infection and disseminated intravascular coagulation. With the recent advance in high resolution ultrasound, the operation became more accurate, easier and safer. In most of the practice

of fetal reduction, fetocide agent (such as KCL) was injected into the chest or heart of the arbitrarily chosen fetuses, through vaginal or abdominal route under ultrasound guidance to decrease the viable fetal number from four or more to two or one.

First reduction in Taiwan The first trial of ultrasound-guided trans-abdominal fetal reduction was performed by Dr. Hsieh and Dr. Liu at National Taiwan University Hospital (NTUH) in 1989. Subsequently, Dr. Ko and Dr. Lien reported their experiences of fetal reduction at NTUH and Provincial Tao-Yuan General Hospital. Usually, KCl was injected into the fetal thorax or fetal heart through vaginal or abdominal route under ultrasound guidance. They concluded that this procedure was quite safe with a low morbidity rate.

Beneficial or not The benefit of selective fetal reduction in pregnancy with four or more fetuses was generally accepted because of the frightening perinatal complications in grand multifetal pregnancy. However, it remains controversial whether triplets warrants fetal reduction. According to the reports by Ng and Chen, 1993, there was no significant difference of the perinatal mortality and morbidity between the triplets doing or not doing fetal reduction. On the other hand, fetal reduction may significantly prolong the pregnancy, increase the birth weight, decrease the necessity of NICU admission, and save the medical cost. In addition, many authors oppose fetal reduction in the triplets because it at least results in an one-third embryonic or fetal loss. Therefore, we need more experiences to make further conclusion.

Twin-Twin Transfusion Syndrome (TTTS)

Twin-twin transfusion syndrome is a severe *in utero* complication of monozygotic twin. It occurs as a result of blood transfer through vascular anastomosis in the placenta (common villous district). Schatz ,1875, was the first to describe the phenomenon of shared circulation between monochorionic twins. Although anastomoses of arteries and veins are present in almost all monochorionic (MC) placenta, it is the anastomosis of an artery to a vein that most likely shifts blood from one twin to the other. Schatz demonstrated that this 'third circulation' usually was accompanied by another arteriovenous anastomosis in the opposite direction which tended to balance the flow and minimize hemodynamic shifts. Depending on the net flow between these anastomoses, mild, moderate or severe TTTS may develop.

Placentation and TTTS Monochorionic-diamniotic (MC-DA) placentation can be diagnosed reliably by assessing placental location and septal membrane thickness using ultrasonography. A few cases of dichorionic (DC) placentation also have very thin septa, and may be incorrectly diagnosed as MC. Likewise, the septum in MC-DA placentation is very thin and may be difficult to detect and some cases are misdiagnosed as MC-MA (monochorionic-monoamniotic). However, MC-DA is rarely misdiagnosed as DC-DA. (Machin GA,1995)

Most of the authors aggreed that TTTS occurred only in MC-DA twins. The frequency of MC-DA twinning in North America and Europe was about 23.1%. (Machin GA,1995) The relative frequency of twinning by chorionicity and amnioticity is still lacking in our country.

Diagnosis of TTTS   TTTS should be suspected if the ultrasonography of one twin pregnancy showed a single placenta, thin intermembrane, same fetal sex and discordance of growth. Occasionally, different sac size with hydramnios/oligohydramnios would be present. Elliott in 1992 divided TTTS to three functionally different categories based on severity of the process and need for therapy to change outcome.

Stuck twin   The most severe form of TTTS, presents as a 'stuck twin' in the second trimester, usually before 20 weeks of gestation, with growth discordance, oligohydramniotic donor and polyhydramniotic recipient. Onset is usually sudden, often with spontaneous premature rupture of membranes (PROM) and/or premature labor and even both intrauterine fetal deaths (IUFD). Recipient or both twins may be hydropic. It is also called 'acute TTTS'. Fetal mortality is near 100% without active management.

There are three associated syndromes in TTTS worth mentioning here:

1. **Twin-reversed arterial perfusion (TRAP)**   Twin-reversed arterial perfusion (TRAP), or acardiac monster, or holoacardius acephalus, results from the early, large, direct A-A and V-V anastomoses between the two cords. As the cardiac function of acardiac fetus declines, its circulation is dominated by that of the 'pump' twin. Arterial flow in the acardiac cord is reversed, flowing from the placenta to the acardiac twin. Perinatal mortality and morbidity are high in the 'pump' twin.

There were five cases of acardiac monsters delivered at NTUH in recent 5 years. The average period of gestation was 33.4weeks . Preterm labor occurred in all cases. Polyhydramnios was noted in 4 cases(80%) and one of them needed weekly aggresive amniocentesis to re-

lieve maternal intra-abdominal pressure which disable her and to prevent preterm labor. One patient suffered from preeclampsia. 4 patients (80%) recieved cesarean section due to difficulty in delivering the hydropic monsters (three cases) or previous sections (one case). One 'pump' twin died in utero at the 35th week, and two died of DICs within 3 days after deliveries. Only two babies survived without major morbidities. The perinatal mortality was 60%.

2. **Acute reversed shunting during delivery in TTTS**   It may occur after the cord clamping of the first-born twin, the blood in the placental parenchyma drains back into the second twin during the delivery interval. The chronic 'stuck' donor twin is less accessible and is likely to be born second, either by vaginal or cesarean delivery. In the presence of superimposed acute reversed shunting, the chronic donor may become acute recipient that appear paradoxically plethoric. In our series of 'stuck twins' , three cases (30%) of the donors has greater value of hemoglobin than the recipients immediately checked after their births. (1.7, 1.9 and 3.7 respectively)

3. **One IUFD in TTTS**   Intrauterine death of one twin in TTTS is a difficult situation with a high morbidity and mortality. Subsequent intrauterine death or immediate neonatal death due to severe anemia of the alive cotwin was noted in severe or moderate TTTS. In mild TTTS, the alive twins were born with a macerated co-twin, but evidences of severe anemia and disseminated intravascular coagulation (DIC) were noted. Multicystic encephalomalasia occurred in one surviving cotwin after delivery. (Jou HJ, 1994) Reversed shunting in TTTS was demonstrated using antenatal doppler ultrasonography, which might explained the neonatal anemia in the surviving

cotwin (mostly the recipient). (Jou HJ, 1993)

The Management of Severe TTTS Five options for active management have been reported in recent years: i.e. *maternal digoxin therapy* for fetal cardiac failure, *indomethacin therapy* for polyhydramnios, *selective fetocide, aggressive amniocentesis* and *selective coagulation of communicating vessels.* The aggressive therapeutic amniocentesis is considered the most effective and least harmful procedure in treating severe TTTS. Overall survival following amniocentesis is 48% (96/196) from the literature. Recent result of amniocentesis in treating 'stuck twin' at NTUH was 62.5%(15/24) survival, compared with 0% survival(0/6)

without intervention. Normalization of amniotic fluid was achieved in 9 patients (75%). The pregnancies were prolonged for seven and 5/7 weeks. No significant complications were noted except one PROM 2 days after the procedure. Although the perinatal outcome was much improved after the therapeutic amniocentesis (from 0 to 62.6%), significant morbidities still took place including necrotizing enterocolitis, renal cortical necrosis and cerebral palsy, etc. in 10 babies (42%). No obvious 'catch-up' growth were noted in the discordant small donors after the long run. The presence of hydrops fetalis or preterm labor at initial diagnosis of TTTS heralds poor prognosis.

Discussion

The decline in twin and triplet rates in Taiwan between 1950s and 1973 may be due to the decrease in parity as a result of introduction of family planning and birth control program. On the other hand, the striking increase in multifetal pregnancy since 1981 to date may be contributed by the use of ovulation-inducing drugs and further assisted reproductive technology(ART).

As we know that ART increases the multiple pregnancy rate by increasing the numbers of fertilized eggs Most of the twin pregnancy from ART should be dizygotic (DZ). It was clearly shown in our data that ART could raised the DZ rate from 28% (exclude ART) to 51%(with 30.7% of all twins made by ART). However, the average DZ was still lower (about 40%) than the United States and the Belgium where twin pregnancy rate were higher(about 21.5/1,000 births), which revealed the racial infuence on the total twin rate and fetal dizygosity.

Previous studies indicated that the maternal age and birth-order effect on the twinning incidence was most pronounced for DZ

twins, with little or no difference for MZ twins. However, recent data in Taiwan showed that both the MZ and DZ twins increased with parity and decreased with maternal age. In the study by Chen CJ, 1992b, the MZ and DZ rates on the adjustment for the effect of parity, were negatively associated with maternal age.

The positive influence of parity on the twinning rate were also shown in the British and America. But divergent results were shown in the foreign literature about the influence of the maternal age on the twinning rate. In Danforth's series (1990), the incidence of twinning increases with mother's age up to 35-39 years, and then declines. This increase, and the subsequent decline has been attributed to the rise in the level of gonadotropin secretion with age, with maximum stimulation of follicles at ages 35-39, and a subsequent decline in ovarian function at older ages. Waterhouse analyzed the total births of England and Wales between 1938 and 1948, 10-year period, got similar findings. However, recent

data from the USA (Taffel, 1995) shows that only in the first births does the twinning rate increase with maternal age. After live-birth order one, the rates either remain approximately at the same level (order two) or are falling (order three or more). The latter result is more compatible with our recent report. There are many differences in the status of the women and their reproductive behavior between the two halves of the century (women in 1938 or 1990), and much of this change may relate to availability of contraception, first-birth age, artificial abortion, infertility treatment, smaller family size and probably other factors as well, which could remarkably modify the twinning process. Of course, further study is needed to clarify these effects on the epidemilogy of twinnings.

ART has affected the rate of multiple births in two ways. First, the procedures themselves directly impact on the incidence of multiple pregnancy; second, the number of patients undergoing infertility treatment has increased dramatically. The latter factor undoubtedly has a greater influence on the overall number of multiple births. In addition, the incidence of multiple gestation is strongly associated with the number of eggs/embryos per tubal/uterine transfer. As the number of eggs/embryos simutaneously trasferred increases, the multiple pregnancy rates rise steeply. The 'ideal' maximum number of eggs/embryos per transfer in a center should be based on the point at which a balance exits between an 'adequate' pregnancy rate and an 'acceptable' incidence of multiple gestations.

There is a distinct difference in the sex ratio at birth for twin and singleton. The proportion of males decreases with each increase in the number of fetuses per pregnancy. It is especially true for the MZ twins. In the East Flanders Prospective Twin Survey (EFPTS) series, the sex proportion of the DZ twins and the singletons did not differ significantly. (Derom R,1995) A possible explanation for these phenomena is that the female-producing zygote has a greater tendency to divide into twin or triplet pregnancy. The question remains, however, as to the explanation and whether the differences could throw some light on the mechanisms of the twinning process.

The perinatal mortality rate, which rises progressively as the number of fetuses increases, had been demonstrated by Botting, 1987. The mortality rates were 6.3%, 16.4%, 20.0%, 21.4% and 41.6%, respectively, among twins, triplets, quadruplets, quintuplets, and sextuplets. Similar result was shown in our recent data (5.4%, and 12.1%, respectively, for twins and triplets).

Several factors are thought to be of relevance for increased perinatal mortality and morbidity in cases of multiple gestation as compared with singleton pregnancies. In most cases, the reason for this excess in perinatal mortality is prematurity secondary to preterm labor, with the second most important factor being intrauterine growth retardation (IUGR). Hypertension, anemia, and birth trauma also are mentioned as possible factors. However, no comparative study of the incidence and distribution of the neonatal morbidity between the twins and singletons has been conducted before. It has been reproted in the literature that pregnancy-induced hypertension (PIH) is more frequently found in twins, so that the neonatal neutropenia and/or thrombocytopenia secondary to maternal PIH also are more frequently encountered in twins. Neutropenia will make the neonates 4 to 8 time-susceptible to bacterial infection.

The risk of extreme prematurity is directly proportional to the number of fetuses within the uterus. Reduction in the number of the fetuses has been proposed as a means to improve perinatal outcome in grand multifetal pregnancy. Selective termination was first described in 1978 by Aberg et al. They

reported a successful selective termination of a twin with Hurler's syndrome. In the second report about this issue, Beck ,1980, performed a hysterotomy at 22 weeks of gestation to remove the affected fetus, and which resulted in a term delivery of a normal child.

The initial report of first-trimester reduction of grand multifetal pregnancies (three or more fetuses) was published by Lopes et al in 1985. From then on, many authors had written their results. Transcervical aspiration or thoracic puncture under ultrasound-guidance was the initial method, but more centers at the present time would prefer transabdominal thoracic punture to avoid the risk of infection and uteroplacental bleeding.

Patients who undergo selective fetal reductions to twins should be treated as if they had conceived two fetuses, with two extra considerations. First, the maternal serum alpha-fetoprotein (MSAFP) will be abnormally elevated after fetal reduction with the presence of the dead fetus. It should be adjusted during risk evaluation for maternal serum screening for Down's syndrome (MSSDS) and also when performimg ultrasonographical screening for fetal morphological abnormalities. Second, regular monitoring for uterine activity begining at about 20 weeks' gestation should be recommended to provide earlier awareness of premature labor, which may be a remote adverse effect from fetal reductions.

Experiences suggest that perinatal outcome are likely to be improved when pregnancies with four or more fetuses are reduced to smaller numbers. However, the advantages of reducing fetal number in triplets are not clearcut, although the outcome is encouraging. Because the number of cases reported prior to the use of ART is limited by the low natural incidence of high order multifetal preganacies, and most published reports only present perinatal mortality, with very little attention given to perinatal mor-

bidity or long-term follow up of the survivors, the accurate data about the outcome of grand multifetal pregnancies is limited. Currently, long-term follow-up data in reported triplet series are insufficient to determine whether first-trimester reduction procedures are truly beneficial.

Studies of clinical outcomes in multiple pregnancies depend heavily on the zygosity and also of chorionicity. As mentioned above, MC twins (who are all MZ) are at higher risk of perinatal complications compared to the singletons. The major differences between MC and DC twins are almost related to the fact that the MC placenta is truly a single placenta perfused by two fetuses. The inter-fetal vascular anastomoses (IFVA) within the MC placentas largely determines the poorer outcomes of MC pregnancies, including various forms of twin-twin transfusion syndrome (TTTS).

IFVAs are of three types, and any combination of the three may be seen in any MC placenta. The three types of IFVA are:

(1) Arterio-arterial anastomoses (A-A): frequently seen (70%) in the chorionic plate

(2) Veno-venous anastomoses (V-V): rarely seen (23%) in the chorionic plate

(3) Arterio-venous anastomoses (A-V): not in the chorionic plate; they represent normal artery-capillary-vein flow in a perfusion zone (e.g. a cotyledon); however, the arterial inflow is from one fetus, while the venous return is to the other twin. It is seen in 48% of MC placenta. The most common pattern is a combination of A-A and A-V anastomosis (83%). (Machin GA, 1995)

It is possible that A-V anastomoses represent perfusion zones in which the chorionic arterial trees of the two twins are roughly equal, but the venous zone of the one (recipient) is larger than that of the other (donor). This anatomical arrangement allows the 'recipient' to receive venous blood in a

zone that is arterially perfused by the 'donor'. If uncompensated, TTTS occurs.

It should be stated here that the vascular patterns observed in the MC placentas after birth do not necessarily accurately reflect the anatomy at all times in the uterus. Changes in vascular pattern do occur, as reflected in well-documented cases of spontaneous resolution of TTTS. And of course, the development of polyhydramnios will modify the structure and function of vascular status.

There are no simple criteria for the diagnosis of TTTS in the prenatal twin. Growth discordance may be caused by unequal venous sharing without TTTS. Hydramnios may result from fetal malformation. Hydrops may be due to a number of factors other than TTTS. Recently we developed a method of prenatal diagnosis of TTTS by Doppler ultrasound quantitative measure-ment of fetal umbilical vein (UV) and descending aorta (DA) blood flow. Intertwin UV-DA ratio (UV/DA) and intertwin UV flow differences could determine the presence of TTTSs and their current severity during the time of initial diagnosis and the degree of improvement after the therapeutic amniocentesis. We will published the data soon.

Sometimes, one twin may die *in utero,* although the actual incidence is not clear. Complications occur in the surviving MC twin. (most of the authors agree that DC co-twin is less risky in same situation) The surviving MC twin is at risk for at least two possible reasons:

(a) The placental parenchyma, previously perfused by the deceased twin, may act as a pool for blood from the surviving twin. Organ infarction occurs and even the survivor dies if the hypotension and hypovolemia are too severe.

(b) The deceased twin may liberate thromboplastins, which result in DIC of the surviving twin.

This can explain the subsequent IUFD or immediate neonatal death of the surviving twin in severe TTTS, and on the other hand, DIC and sequele of so-called 'twin-embolization syndrome' take place in the milder cases of TTTS. In the second trimester, when the one fetus dies, the surviving twin may develop aplasia cutis congenita and multiple bowel atresia. While in the third trimester, visceral infarction may involve lungs, kidneys, liver and brain.

In case of severe TTTS, expectant management generally results in 100% mortality. Active management can actually improve the outcome by several means. At present, therapeutic amniocentesis has the best result and is safest. Because TTTS does not exist without IFVAs, only the method which directly aims to the interruption of the pathogenesis would have the best effect. Some effort should be done to (1) halt the one-way transfusion including nutrients; (2) improve their intrauterine environment; (3) prolong the pregnancy; and (4) prevent the passage of debris or shock should one twin die. (De Lia JE,1995) Selective laser coagulation theoretically has better effect, but is somewhat excessive. More accurate mapping of the sites of A-V anastomoses will be required to fulfill this job without jeopardizing the continuation of the pregnancy or risk the future reproductive capability of the mother. This procedure is considered experimental at present and it is not clear that results by this method are superior to those from aggressive amniocentesis.

When the diagnosis of a multiple gestation is made, the parents may have many fears concerning: the addition of more than one baby to the family; being unable physically and emotionally to care for more than one infant; financial concerns for the cost of caring for more than one baby and increased hospitalization of the mother and her infants. The parents probably recognize that there is a higher risk for prematurity and other ma-

ternal and fetal complications. Some of the minor discomforts of pregnancy become exaggerated with a large uterus. The awkwardness and discomfort may lead to difficulty in sleeping. These women also may be depressed by their large size and may be anxious over their weight gain. Medical, psychological and socioeconomical supprot are all very important for these lovely women.

Further work is needed for the study of multiple pregnancy, not only from the obstetric point of view, and also from the epidemiological, nursing and sociofinancial point of view. We hope that more investigators will join.

台灣之多胞胎妊娠

前　　言

　　幾乎在所有的文明中，生育能力都負有其獨特的意義。婦女生兒育女的能力對其性別認同與自尊是非常重要的，不能生育固然會影響女性的自尊與自我認同，然而過度的生育力(例如多胞胎妊娠)也可能有不良影響。

　　大家都知道多胞胎的胎嬰兒死亡率與致病率較單胞胎爲高，但是有關台灣地區多胞胎妊娠的發生率流行病學以及致病率與死亡率的資料卻極有限，因此我們收集整理相關的本土性資料並報告近年的研究進展。

　　近來由於不孕症專家及實驗室的數目快速增加，而人工協助生殖技術也大爲普及，對於雙胞胎與多胞胎的生態學有相當大的影響。由人工協助生殖技術所產生的超多胞胎使醫界必需進行減胎術以避免因極度早產所造成的危害。本文將討論多胞胎之減胎術並探討未來的研究方向。

　　最後我們將談到可造成高致病率與死亡率的雙胞胎間輸血症候群，我們將討論其致病機轉與臨床徵象。近來有資料顯示積極處理雙胞胎間輸血症候群可能有所助益，但未來努力的方向將是設法矯正造成此症候群的病理過程。

流行病學

　　多胞胎妊娠的發生率在最近幾年有增加的現象。由 1950 年代至 1973 年其發生率逐漸下降， 1974 至 1980 年稍有增加並維持不變，到了 1981 至 1990 年則明顯增加(Chen CJ,1992a)(圖 1,2)。據台北市四家醫院的統計，在 1985 年十月至 1989 年六月間雙胞胎的發生率爲每一千個生產中有 11.5 例(844/73264)。根據 Weinberg's 法則(異卵雙胞胎的數目爲不同性別雙胞胎的兩倍)推論同卵雙胞胎的發生率爲 7.5/1000 ，異卵雙胞胎則爲 4.0/1000 。最近五年雙胞胎發生率有再上升的情形，台大醫院在 1991 年一月至 1995 年四月之間雙胞胎發生率爲 2.15%(243/11309)，如果將人工協助生殖技術所造成的雙胞胎排除則發生率爲 1.41%(158/11224)。在長庚醫院也有相同的趨勢，於 1990 年七月至 1995 年十月間雙胞胎的總發生率爲 1.48%(364/24648)，經排除人工協助生殖技術所引起者後，其發生率爲 1.26%(309/24593)。若將馬偕醫院的資料列入統計，則台北市雙胞胎的

總發生率為 1.55%(表 1,2,3)。若將人工協助生殖技術所產生的雙胞胎排除,則自然發生雙胞胎的機率為 1.3%,三胞胎的總發生率為 0.14%;若將人工協助生殖技術所造成的排除之後,發生率將為 0.019%。四胞胎的發生率為 0.015%,全部都是人工協助生殖技術的結果。

<u>配型(Zygosity)</u>　　只有少數研究探討雙胞胎的配型。配型通常可由胎兒性別、胎盤情況與紅血球抗原來判定。在美國,約有三分之一的雙胞胎為同卵雙胞胎,但在台灣同卵雙胞胎的比率似乎較高,不論是由 Weinberg's 法則或實際的統計,其百分比分別為 56%(Teng RJ,1994), 60%(CGMH),到 66%(Chen CJ,1992b)。 人工協助生殖技術會影響異卵雙胞胎的比率,台大醫院近五年的資料顯示異卵雙胞胎佔所有雙胞胎的 51%(其中有 30.7%是經人工協助生殖技術而產生),若將人工協助生殖技術所造成之雙胞胎排除之後,異卵雙胞胎佔 28%(表 2)。假設有 15%的雙胞胎是由人工協助生殖技術所造成(此與長庚醫院近五年的統計相符),則異卵雙胞胎的比率將為 39%,而同卵雙胞胎則為 61%;此值將與其他學者的報告相類似。

<u>胎次與母親年齡</u>　　雙胞胎發生率隨胎次增加而增加,但隨母親年齡增加而減少(表 4)。同卵與異卵雙胞胎的比率亦隨胎次而增加,但隨母親年齡增加而減少。父親的年齡在雙胞胎與單胞胎間並無顯著差別。

<u>人工協助生殖技術</u>　　近年來有相當部份的多胞胎是因人工協助生殖技術所造成的。長庚醫院統計人工協助生殖技術由所造成的雙胞胎佔所有雙胞胎的 15.1%(55/364);在台大醫院此比率則為 30.7%(70/228)。台大醫院所有的三胞胎都是由於人工協助生殖技術所造成的(19/19);在長庚醫院則為 61%(11/18)(表 3)。

<u>男女嬰比率</u>　　雙胞胎中男嬰與女嬰的比率為 1.03(671/651)(Hsieh TT,1992),而在單胞胎中則為 1.08(Hsieh TT,1991)。據 Teng 之統計,雙胞胎男與女之比率更低達 0.93(表 5)。在自然發生的妊娠中,當子宮內胎兒的數目增加時男嬰所佔的百分比有下降的趨勢(表 6);可能的解釋為發育成女性的配子較易自然發生分裂。相反的在異卵雙胞胎中男嬰與女嬰的比率較同卵雙胞胎高(表 7)。

　　在經由人工協助生殖技術而成功的妊娠中,男嬰所佔的比率較高。台大醫院統計經人工協助生殖技術受孕所致的三胞胎中,男嬰與女嬰的比率為 1.32;長庚醫院所統計的

男女比率則爲 1.20(表 8)。長庚與台大醫院統計經人工協助生殖技術所致之雙胞胎之男女比率爲 1.19 及 1.12，此比率仍較單胞胎或所有雙胞胎的男女比率爲高。當然在人工協助生殖技術操作過程中男嬰的比率可能上升，然而有意思的是在各種人工協助生殖技術中，男女比率最低的(0.84)見於體外受精後的懷孕，可能在體外的微環境對要形成男性的配子有不良影響。（表 9）

周產期死亡率與致病率

早產　　多胞胎妊娠發生早產(懷孕滿 37 週以前生)的機率較大。三胞胎與雙胞胎妊娠發生早產的機率分別爲 75% 與 36.9%，而單胞胎則只有 5.6%(臺大醫院、長庚醫院，Hsieh TT,1991,1992)。 Teng 在 1994 年也有類似的報告。三胞胎兒出現低出生體重(小於 2500 公克)的發生率爲 79.6%，在雙胞胎及單胞胎的發生率分別爲 47.9% 與 5.9%。單胞胎的平均妊娠期爲 39.2 週，雙胞胎與三胞胎則爲 36.5 週與 32.6 週(表 10)。

呼吸窘迫症候群　　呼吸窘迫症候群乃是因爲早產與低出生體重所造成的，爲雙胞胎最常見的新生兒併發症，發生率約爲 8%(Ho SK,1975;Lai YC,1994)。幾乎所有的呼吸窘迫症候群都發生於懷孕 36 週以前出生，且出生體重不足 2000 公克者。後出生的雙胞胎發生呼吸窘迫症候群的機率較先出生者高，多數新生兒病變都與呼吸窘迫症候群有關，如腦室內出血、慢性肺病、早產性視網膜病變等。三胞胎發生呼吸窘迫症候群的機率更高 (20%)。

死亡率　　雙胞胎之新生兒死亡率由每一千個活產中 18 例(Hsieh TT,1994)到 47 例(Lai PC,1994)。大多數發生於懷孕滿 32 週以前，且出生體重極低(小於 1500 公克)的胎兒。雙胞胎的周產期死亡率爲 54/1000，三胞胎則爲 121/1000(Chen CJ,1992a;台大醫院，長庚醫院,1995)。

配型　　雙胞胎之配型會影響其周產期死亡率。 Chen(1992a) 在台北市所做的研究顯示同卵雙胞胎、異卵雙胞胎與單胞胎的周產期死亡率分別爲 7.5%，1.4% 與 0.7%。與單胞胎相比的話，同卵與異卵雙胞胎發生周產期死亡的相對危險性分別爲 10.0 與 1.9。雙胞胎發生周產期死亡的一致性(雙胞胎兒之一在子宮內死亡時，另一胎兒的周產期死亡率)在同卵雙胞胎爲 60%，在異卵雙胞胎爲 0%。同卵雙胞胎的胎膜爲單絨毛膜的機會較

大，胎盤內血管吻合的機率較高，因此較易發生雙胞胎間輸血症候群與其他產科併發症；此點可部份解釋為何同卵雙胞胎有較高的周產期死亡率與雙胞胎兒一致死亡的情形。

<u>剖腹產率</u>　雙胞胎之剖腹產率較高，在 1983 至 1985 年間為 44.2%，在 1989 至 1991 與 1990 至 1995 年間分別為 77.2%與 92.9%(Lai PC,1994;長庚醫院,1995)。剖腹產率的增加，可能反映出目前產科醫師處理雙胞胎的態度。雖然雙胞胎的死亡率較高與早產有關，但與生產方式可能也有些關係。在 Lai 的統計中，懷孕 27 至 32 週之間出生，或出生體重在 1000 至 1499 公克之間時，陰道生產的死亡率較高，而後出生的雙胞胎兒死亡率尤其高。

<u>出生順序與致病率</u>　1971Ware 發現經翻轉與臀位胎兒取出術生下來的第二個雙胞胎的一分鐘 Apgar score 較低。1988Ghai 與 Vidyasagar 也發現後出生的雙胞胎兒五分鐘的 Apgar score 較低。Lai(1994)發現後出生的雙胞胎兒發生透明膜病變與新生兒死亡的機率較高，特別是當懷孕週數不足 32 週或出生體重低於 1500 公克時。同篇研究也發現陰道生產較剖腹生產者有較高的死亡率與致病率，因此他建議當懷孕週數小於 32 週或預測出生體重不足 1500 公克時應行剖腹產。

先天畸形

<u>盛行率</u>　雙胞胎發生重大先天畸形的盛行率較單胎高，這些畸形包括有無腦症、水腦症、腦膜膨出、兔唇、顎裂、先天性心臟病、肛門閉鎖、尿道下裂、杵狀足、遠端肢體異常、染色體異常、無心畸胎、連體嬰及其他畸形。台大醫院近五年來雙胞胎合併先天畸形的機率為 2.1%，較單胎的 1.13%為高(Shyu MK,1992)。長庚醫院近五年來雙胞胎合併先天畸形的機率為 1.5%。在 Chen 的研究中(Chen CJ,1992a)，雙胞胎發生重大先天畸形的機率為 2.1%，約為單胎妊娠的四倍(0.6%)。同卵雙胞胎發生重大先天畸形的機率(2.7%)較異卵雙胞胎(1.0%)高，同卵與異卵雙胞胎發生重大先天畸形的相對危險性各為單胎的 4.6 與 1.7 倍。上述結果與先前的研究結果相符，顯示雙胞胎妊娠時子宮內環境導致發生先天畸形的不良影響。

<u>一致率</u>　Chen 的研究亦顯示同卵雙胞胎發生重大先天畸形的一致率(18%)較異卵雙胞胎

(0%)高。同卵雙胞胎發生顏面裂的一致率為29%，較其他國家先前的報告低。由於同卵雙胞胎發生顏面裂的一致率不是 100%，顯示造成顏面裂的機轉中，子宮內環境的影響可能較遺傳因素來的重要。

連體嬰　連體嬰乃是同卵雙胞胎所發生最糟糕的畸形，它是在胚胎形成兩個胚胎平盤後發生不完全分裂所造成的。連體嬰的盛行率在各個國家各不相同，在台北市統計的盛行率為每十萬生產中有 2.7 例，但最近五年在台大醫院的統計則高達每十萬次生產 26.5 例，可能因該院為轉診中心之故。

　　1979 年一對出生於台中的坐骨連體嬰接受外科分割手術，然而兩個雙胞胎都合併有重度殘障。 1981 年陳、謝、黃等人報告首例於懷孕二十八週時產前診斷出來的臍連體嬰，此例連體嬰於懷孕三十五週時生產，並經順利分割，兩個小孩都健康。在 1980 年代另有四例連體嬰經產前診斷出來，但都是在懷孕的最後三個月；由於腦部或心臟的相連，這四對連體嬰都未能手術分割。到 1990 年代仍有散在性的報告產前診斷出來的連體嬰，此期間發現連體嬰的時機通常是在懷孕第二個三月期的早期，且通常於發現後終止妊娠。

子宮內生長與生長速度的不一致性

出生體重　　　雙胞胎兒的生長速度較單胞胎來得慢，在懷孕 33 週前，雙胞胎兒的平均出生體重與單胎者類似，但到懷孕 37 週後，雙胞胎兒的平均出生體重將會降至單胞胎兒的十個百分位以下(Teng,1994)。據長庚醫院統計的 661 對雙胞胎(Hsieh TT,1992)顯示雙胞胎在懷孕 33 至 35 週成長最快，平均每週長 200 公克；在懷孕 28 至 32 週以及 35 至 38 週每週長 145 公克；到 38 週以後平均出生體重每週只增加 35 公克。與單胞胎相比的話，雙胞胎兒在懷孕 28 至 32 週時的平均出生體重約低 100 公克，此後兩者的差異逐漸擴大，到足月時相差約 500 公克(Hsieh TT,1992)。

出生順序與胎兒體重　　　有兩篇報告顯示，在台灣先出生的雙胞胎兒的平均體重(2459+537 公克)較後出生者(2402+548 公克)為重(Hsieh TT,1992)。後出生的雙胞胎合併低出生體重(<2500 公克) 的機率較先出生者為高(50.5%比 45.2%)。然而在懷孕週數相同的雙胞胎兒間，其出生體重與出生順序並無顯著差異。平均出生體重差異(雙胞胎兒間體重差異 / 較重胎兒之出生體重)在 Hsieh(1992)與 Lai(1994)兩人的報告中分別為

11±10%與 10.4±9.0%。

<u>胎兒性別與出生體重</u>　　男性雙胞胎兒的平均出生體重(2476±527 公克)較女性雙胞胎兒(2386±555 公克)重，而女性雙胞胎兒合併低出生體重的機率較男性雙胞胎兒高(Hsieh TT,1992)。

<u>生長差異與新生兒期異常</u>　　在雙胞胎妊娠中常可發現兩個胎兒的生長速度不等，平均之不一致性大約在 10.4±9.0%至 11±10%之間；而通常先出生者較後出生者重。有研究顯示當雙胞胎兒出生體重差異超過 15%以上時，較易發生不良情況，且特別可能發生於較小的那個胎兒(Hsieh TT,1994)。體重不足 2000 公克之較小的雙胞胎與相同懷孕週數但體重超過 2000 公克者相比的話，其發生新生兒期異常的危險性將高達十倍。懷孕不足 34 週的雙胞胎與懷孕超過 34 週但出生體重相同的雙胞胎相比的話，發生新生兒期異常的危險性高五倍。經邏輯回歸分析後發現，決定是否發生不良情況的乃是出生體重與懷孕週數，而不是雙胞胎兒間的生長差異。

多胞胎妊娠與減胎術

隨著人工協助生殖技術的蓬勃發展，多胞胎妊娠的發生率急速上升。由文獻上得知雙胞胎、三胞胎與四胞胎的平均懷孕週數分別為 37,33 與 31 週，可見多胞胎兒的胎兒數目愈多，懷孕期間愈短。三胞胎與四胞胎的預後將隨早產與其他併發症而變差，此為產科醫師所面臨的重大挑戰。

<u>減胎術</u>　　1985 年 Lopes 等人首先報告在多胞胎妊娠時，選擇性地終止妊娠的技術。然而此種手術常合併有羊膜破裂、流產、感染與瀰漫性血管內凝血等併發症。近年隨著高解析度超音波的發明，使減胎術變得更精確、簡單與安全。大部份用來殺死胎兒的藥劑(如 KCl)都是注射入隨機選擇出來的胎兒的胸腔或心臟內，手術需在超音波導引下進行，可選擇經由腹部或陰道來注射藥物，其目標乃是希望將存活胎兒的數目減到兩個或一個。

台灣首例在超音波導引下經由腹部進行減胎術乃是於 1989 年由謝豐舟與劉志鴻在台大醫院施行。其後柯氏與連氏也報告在台大醫院與省立桃園醫院行減胎術的經驗。手術通常在超音波導引下經由腹部或陰道將 KCl 注入胎兒胸腔或心臟內。其結論為減胎術

是安全的且合併症發生率很低。

<u>減胎術是否有好處</u>　　在四胞胎或更多胎時常合併有嚴重的周產期併發症，多數人認為選擇性的減胎術是有好處的。至於三胞胎是否需行減胎術仍有爭議。據 1993 年吳氏與陳氏的報告，在三胞胎時施行減胎術對周產期死亡率與併發症並無顯著差別，然而減胎術可顯著地延長懷孕、增加出生體重、減少必需住進新生兒加護病房的機率，同時亦可降低醫療費用。然而因為減胎術至少造成三分之一的胚胎或胎兒的喪失，有些專家反對在三胞胎行減胎術。目前仍需更多經驗才能對此做出結論。

雙胞胎間輸血症候群

　　雙胞胎間輸血症候群是發生於同卵雙胞胎間的嚴重子宮內併發症，它是因為胎兒血液經由胎盤上之血管吻合(共同絨毛區)傳送所引起的。 1875 Schatz 首先描述此同卵雙胞胎間共同血液循環的現象。雖然幾乎所有的同卵雙胞胎的胎盤都有血管吻合的情況，但只有當動脈與靜脈有吻合時才最容易發生血液由雙胞胎之一傳送至另一胎兒的現象。 Schatz 證實在此第三循環狀況存在時，通常會合併有另一流向相反之動靜脈吻合以平衡血流並減少血液動力學上之變化，此吻合間血液之總流量將決定引起的是輕度、中度或重度雙胞胎間輸血症候群。

<u>胎盤狀況與雙胞胎間輸血症候群</u>　　目前可利用超音波看胎盤位置與雙胞胎間胎膜厚度來診斷是否為單絨毛膜-雙羊膜胎盤。少數雙絨毛膜胎盤可能會有很薄的胎膜，因而易被誤認為單絨毛膜。而單絨毛膜-雙羊膜胎盤也可能因胎膜過薄未被發現，而被誤診為單絨毛膜-單羊膜胎盤。然而單絨毛膜-雙羊膜胎盤很少被誤診為雙絨毛膜-雙羊膜胎盤。

　　大多數人相信雙胞胎間輸血症候群只發生於單絨毛膜-雙羊膜胎盤。在北美與歐洲，單絨毛膜-雙羊膜胎盤佔所有雙胞胎的 23.1% (Machin GA, 1995)，在台灣則尚未有相關的資料。

<u>雙胞胎間輸血症候群的診斷</u>　　假使在超音波下發現雙胞胎，且見在兩個胎兒間只有單胎盤及較薄胎膜，胎兒性別相同而胎兒大小差異很大時，應考率是否有雙胞胎間輸血症候群。有時可見兩個胎兒之羊膜囊大小不等，並合併有羊水過多或過少現象。 Elliott 在

1992 年依雙胞胎間輸血症候群不同的嚴重程度及是否需要治療，而將其再細分為三類。

被困住的雙胞胎(Stuck twin) 最嚴重的雙胞胎間輸血症候群稱為被"困住的雙胞胎"，發生於懷孕的第二個三月期，通常於二十週以前出現，將會造成雙胞胎間體重不一致的現象，供血者出現羊水過少，受血者則羊水過多；症狀通常突然發作，常合併有早期破水與/或早產，甚或造成兩個胎兒都死於子宮內，此時受血者(或兩個胎兒)可能出現水腫，這種情況也稱急性雙胞胎間輸血症候群，若未經積極治療，胎兒幾乎百分之百死亡。雙胞胎間輸血症候群可能合併下列三個症候群

(一) 雙胞胎動脈灌注逆流 或稱無心畸胎或無頭全無心畸胎，乃是因懷孕早期雙胞胎臍帶間有大的動脈-動脈與靜脈-靜脈吻合所造成，當無心畸胎的心臟功能逐漸降低時，其循環功能主要由另一胎兒來提供，因此無心畸胎臍帶的動脈血液流向逆轉，變成由胎盤流向無心畸胎。此時另外那個正常的胎兒也將會有很高的周產期死亡率與致病率。近五年在台大醫院有五例無心畸胎，全部都是早產，平均懷孕週數為 33.4 週。四例合併有羊水過多症，其中有一例甚至需要每週施行羊膜穿刺術放水，以解除孕婦的不適症狀並避免早產。合併子癇症者有一例。四例以剖腹生產，三例係因胎兒水腫而造成難產，另一例則是因前次剖腹產而開刀。提供心臟功能的胎兒有一例於懷孕 35 週發生子宮內死亡，另有兩例因合併瀰漫性血管內凝血於出生後三天內死亡，只有兩例存活下來且未發生重大併發症，這些胎兒的周產期死亡率為 60%。

(二) 生產時急性逆向分流 當先出生的胎兒臍帶被夾住後，胎盤的血液可能回流至尚未出生的胎兒體內。無論是經陰道生產或是剖腹產，較晚生下來的通常都是供血的胎兒，此時若再發生血液急性逆流，則此慢性供血者可能變成急性受血者，因此於出生後會顯現異常的多血狀況。在我們的統計中有三例(30%)供血胎兒出生後血紅素反而比受血者高。

(三) 雙胞胎之一於子宮內死亡 發生雙胞胎間輸血症候群時，若有一個胎兒在子宮內死亡，另一胎兒將會有相當高的死亡率與致病率。在中度或嚴重的雙胞胎間輸血症候群時，存活的胎兒可能因嚴重貧血而在子宮內或於出生後很快地死亡。若是雙胞胎間輸血症候群較輕微，則胎兒可能與已浸軟的死胎一齊生下來，但常會合併有嚴

重貧血或瀰漫性血管內凝血等現象。 Jou(1994)曾報告一例於存活的胎兒發生多囊性腦軟化的個案雙。胞胎間輸血症候群發生逆向分流現象可以產前都卜勒超音波來證實，由此可解釋爲何存活的胎兒(通常是受血)者會有貧血現象(Jou HJ,1993)。

嚴重雙胞胎間輸血症候群的處理　　有五種積極處理方式可供選擇：(一)於母親身上使digoxin 來治療胎兒的心臟衰竭，(二)使用 indomethacin 來治療羊水過多症，(三)選擇性地殺死其中的一個胎兒，(四)積極性地行羊膜穿刺術放水，(五)選擇性地燒灼雙胞胎間相通的血管。這些方法中可能以積極性的羊膜穿刺最有效、最安全。文獻上報告經羊膜穿刺後胎兒存活的機率爲 48%(96/196)。近年台大醫院以羊膜穿刺術治療"被困住的雙胞胎"，其存活率爲 62.5%(15/24)，而未治療者全無存活(0/6)；其中有九例(75%)羊水量恢復正常而懷孕期平均得以再延續 7 又 5/7 週。除一例在術後兩天發生早期破水外，未有其他重大併發症。雖然在做了羊膜穿刺術後胎兒的周產期預後有相當的改善，但其中十例(42%)新生兒仍發生壞死性大小腸炎、腎皮質壞死、腦性麻痺等重大併發症。經長期子宮內治療後，發現體重較低的供血雙胞胎兒的生長並未能追上受血者。若是在診斷雙胞胎間輸血症候群時已出現有胎兒水腫或早產通常預後都不好。

討　　論

　　1950 年代至 1973 年間，台灣地區多胞胎發生率的下降可能是推廣家庭計劃後胎次減少所致， 1981 年以來多胞胎有明顯的增加，可能是刺激排卵藥物的使用以及其他人工協助生殖技術發展的結果。

　　人工協助生殖技術導致多胞胎增加係由於受精卵數目的增加，因此大多數應爲異卵雙胞胎。在我們的資料中很明顯地看出人工協助生殖技術可使異卵雙胞胎的比率由28%(排除人工協助生殖技術所致者後)增至 51%(其中 30.7%是由人工協助生殖技術所致之雙胞胎)。然而我們平均的異卵雙胞胎的發生率仍比美國比利時等國的報告爲低(約40%)，而在這些地區的雙胞胎發生率也較高(每一千次生產約有 21.5 例)，顯示種族因素對雙胞胎發生率與雙胞胎兒配型的影響。

　　先前的研究顯示母親年齡與胎次對雙胞胎發生率所造成的影響以異卵雙胞胎最爲明顯，對同卵雙胞胎的發生率則影響較小。然而近年台灣的資料顯示不管是同卵或異卵雙胞胎，都隨母親胎次而增加，但隨母親年齡增加而減少。據 Chen(1992b)的研究，在經校正胎次的因素之後，同卵雙胞胎與異卵雙胞胎的發生率與母親年齡呈負相關性。

英國與美國的報告亦證實胎次與雙胞胎發生率的正相關性。至於母親年齡與雙胞胎發生率的關係，文獻上的看法並不一致。 Danforth 報告 35 到 39 歲以前雙胞胎發生率隨母親年齡增加而上升，超過這年紀之後隨年齡增加，發生率反而下降。原因可能是性腺激素的分泌隨年齡增加而上升，但過了 35-39 歲之後則隨著年齡增加卵巢功能逐漸衰退，使促性腺激素的分泌減少。 Waterhouse 分析 1938-1948 年間在英國與威爾斯所有的生產，也得到相類似的結論。然而近年美國 Taffel(1995) 的報告，只有在第一胎孕婦可見到雙胞胎發生率隨母親年齡而上升的現象，在生過一次活產的孕婦，其雙胞胎發生率則維持不變(第二胎)或隨年齡增加而下降(第三胎以後)。後者的結論與我們最近的資料相符。在 1938 與 1990 這兩個不同年代，婦女的處境與生育行為有相當大的差別，例如避孕方式、初次生產的年齡、人工流產、不孕症的治療、小家庭人口數減少等；這些因素都可能改變雙胞胎的形成。但我們仍需更多資料來探討這些事項對雙胞胎流行病學的影響。

　　人工協助生殖技術對多胞胎發生率的影響可分兩方面來看。首先這些技術本身就會增加多胞胎發生的機會，其次接受不孕症治療的婦女人數也有顯著的增加。後者對多胞胎發生數目的增加無疑地有較大的影響。此外多胞胎發生率與植入輸卵管或子宮的卵子或胚胎數目有直接關係，當同時植入的卵子或胚胎數目增加時，多胞胎的發生率也隨之上升。每次治療到底應植入多少卵子或胚胎，除了考率懷孕成功的機率外，也要注意勿使多胞胎的發生率過高。

　　雙胞胎兒與單胞胎的性別比率有明顯差別，當所懷胎兒的數目增加時，男嬰所佔的比率會下降。此現象在同卵雙胞胎特別明顯。 East Flander 前瞻性的雙胞胎調查研究(EFPTS)發現異卵雙胞胎與單胞胎的性別比率並無明顯差別，可能因形成女性的配子分裂成雙胞胎或三胞胎的傾向較強之故。雙胞胎形成的機轉目前仍不清楚，性別差異的現象或可提供我們思考的方向。

　　隨著多胞胎胎兒數目的增加，周產期死亡率也隨之上升。 Botting(1987) 報告雙胞胎、三胞胎、四胞胎、五胞胎、六胞胎之死亡率分別 6.3%,16.4%,20.0%,21.4% 與 41.6% 。我們最近的研究也顯示相似的結果(雙胞胎與三胞胎的死亡率分別為 5.4% 與 12.1%)。

　　造成多胞胎周產期死亡率上升的主要原因為早產，其次為子宮內生長遲滯，高血壓、貧血與生產傷害亦為可能的原因。然而以前並未有比較雙胞胎與單胞胎兒發生新生兒併發症的形態與機率之研究。文獻曾有報告雙胞胎懷孕較易合併妊娠引發之高血壓，因此易造成新生兒中性白血球過低與/或血小板過低，而中性球過低會使新生兒發生細菌

性感染的機率增加四至八倍。

　　極度早產發生的機率與子宮內胎兒的數目成正比，爲改善周產期的預後可考慮設法減少子宮內胎兒的數目。選擇性的減胎術首先由 Aberg 等人在 1978 年提出，他們成功地終止雙胞胎中合併有 Hurler 症候群的那個胎兒。第二例則是由 Beck 於 1980 提出，他於懷孕 22 週時行子宮切開術取出不正常的胎兒，而正常的胎兒則一直等到足月才出生。

　　於懷孕的前三個月對胎兒數目超過三個的超多胞胎行減胎術首先由 Lopes 等人於 1985 年提出，其後有許多專家亦提出他們的經驗報告。早先的作法是在超音波導引下經由子宮頸抽吸或行胸腔穿刺，但目前大多數人採經由腹部進行胸腔穿刺，以避免感染與子宮胎盤出血。

　　對做過選擇性減胎術將胎兒數目減至兩個的孕婦的處理方式與一般雙胞胎孕婦相同，但有兩點要特別注意：(一)行減胎術後，由於有死胎留存於子宮內，母體血清甲型胎兒蛋白會不正常地上升，因此在做母血唐氏症篩檢時應考率此點。此外在做超音波篩檢胎兒形態異常時也要注意。(二)由於減胎術後發生早產機率較大，從懷孕 20 週起應定期監測子宮收縮以期及早發現早產現象。

　　經驗顯示當多胞胎之胎兒數目超過四個時，若能將胎兒數目減少將可改善其周產期預後。至於三胞胎行減胎術是否有好處仍未有定論。在人工協助生殖技術廣泛應用前，自然發生的超多胞胎數目很少，且多數研究只報告周產期死亡率，很少注意到周產期併發症與存活者的長期追蹤，因此目前對超多胞胎的預後所知仍極有限。目前有關三胞胎的長期追蹤的資料仍不是很充足，無法判斷施行減胎術是否有益。

　　多胞胎妊娠的預後與配型及胎膜形態有很重要的關係。單絨毛膜之雙胞胎(全爲同卵雙胞胎)與單胞胎相比的話，有較高的周產期併發症。單絨毛膜與雙絨毛膜雙胞胎的主要差別，乃是單絨毛膜雙胞胎的胎盤實際上是接受兩個胎兒血液灌注的單一胎盤，而單絨毛膜雙胞胎懷孕的預後較差(包括各種不同形式的雙胞胎間輸血症候群)，主要乃是單絨毛膜胎盤上的胎兒間血管吻合所致。

　　胎兒間血管吻合有三種形式，在單絨毛膜胎盤中這三種形式可以任何不同的組合出現。(一)動脈-動脈吻合：常出現在絨毛膜板上(70%)，(二)靜脈-靜脈吻合：在絨毛膜板上較少見(23%)，(三)動脈-靜脈吻合：未見於絨毛膜板上；基本上它是代表絨毛葉內正常的動脈微血管靜脈的血流，但問題在於它是由一個胎兒的動脈流往另一個胎兒的靜脈，此種情形見於 48% 的單絨毛膜胎盤。

　　最常見的是同時合併有動脈動脈與動脈靜脈吻合，約佔 83%。(Machin GA, 1995)

動靜脈吻合可能代表胎盤上的灌注區其絨毛膜動脈分支兩個 胎兒大致相同，但其中一個胎兒(受血者)的靜脈區較另一胎兒(供血者)大，由於此種解剖學上的特性，使受血者可由供血者動脈灌注的區域接受靜脈血，此現象若未經適當代償，將發生雙胞胎間輸血症候群。

要注意生產後在單絨毛膜胎盤上所看到的血管情形並不一定正確反應其在子宮內的解剖情況，血流的情形在子宮內可能發生變化，因此有時可見雙胞胎間輸血症候群能自行消失。而若發生羊水過多症亦可能改變血管的結構與功能。

目前仍然沒有簡單的標準能於產前診斷 雙胞胎間輸血症候群。雙胞胎兒間體重的差異可能由於靜脈血流不平均所造成，而不一定有雙胞胎間輸血症候群。羊水過多可能由於胎兒的先天畸形所造成。造成胎兒水腫的原因很多，並不一定是雙胞胎間輸血症候群。近來我們發展出一套利用杜卜勒超音波定量測量胎兒臍靜脈與降主動脈血流量來產前診斷雙胞胎間輸血症候群的方法，雙胞胎兒間的臍靜脈／降主動脈血流量比值以及雙胞胎兒間的臍靜脈血流量可決定是否有雙胞胎間輸血症候群以及其嚴重程度，同時亦可作為施行治療性羊水穿刺後追蹤雙胞胎間輸血症候群改善的情形的參考。我們近期將發表相關的報告。

有時雙胞胎之一會在子宮內死亡，此種情況的真正發生率仍不清楚。大部份專家同意若是異卵雙胞胎，則存活的胎兒發生併發症的機率較小。但同卵雙胞胎則可能造成併發症，其原因有二：(一)先前由已死亡的胎兒所灌注的胎盤可能成為存活胎兒血液留存的處所，因此存活胎兒可能發生器官梗塞，若低血量與低血壓過於嚴重，甚至可因而造成存活胎兒死亡。(二)死亡的胎兒可能釋出凝血激素，導致存活胎兒發生瀰漫性血管內凝血。上述原因可解釋為何在嚴重雙胞胎間輸血症候群，存活的胎兒會發生子宮內死亡或於新生兒期死亡。而在較輕微的雙胞胎間輸血症候群，則可能發生瀰漫性血管內凝血或雙胞胎栓塞症候群。若是雙胞胎之一於懷孕的第二個三月期死亡，存活的胎兒可能發生先天性皮膚缺損或多發性腸閉鎖；若是發生在第三個三月期，可能造成存活胎兒肺、腎、肝、腦等內臟的梗塞。

在嚴重的雙胞胎間輸血症候群，期待性的處理方式常會造100%的胎兒死亡率。而積極的處理確能改善預後。目前以治療性羊膜穿刺術的效果最好且最安全。若無胎兒間血管的吻合將不會有雙胞胎間輸血症候群，因此只有直接阻斷此種血管的交通，才可能會有最好的結果。此時應做的事項還包括：(一)阻斷單向的輸血與營養的傳送，(二)改善子宮內環境，(三)延長懷孕期間，(四)若有一個胎兒發生子宮內死亡，應避免存活胎

兒接受到由死胎傳送來的物質或發生休克(De Lia JE, 1995)。使用雷射選擇性地對連接兩個胎兒的血管進行燒灼，理論上應會有較好的結果，但為了避免危及懷孕以及維持孕婦未來的生育能力，做此手術前應能準確地將動靜脈吻合處定位出來。目前這種雷射手術仍屬實驗性質，它的效果是否會比積極性羊膜穿刺術好仍不清楚。

當一對夫婦被告知懷多胞胎時他們可能要面臨許多擔憂，例如家中人口一下子增加太多、在體力與心理是否有上能力同時照顧一個以上的小孩、照顧小孩的經費是否足夠、孕婦與小孩住院的次數與天數可能較一般人多等。他們可能認知到懷孕合併早產或其他母體與胎兒併發症的機率較大。由於子宮擴大情況較單胎者厲害，懷孕期間的不適將更明顯，可能影響到睡眠。孕婦也可能因體型改變太多而憂鬱或因體重增加太多而擔心。對這些孕婦提供醫學上、精神上及社會經濟上的支持是非常重要的。

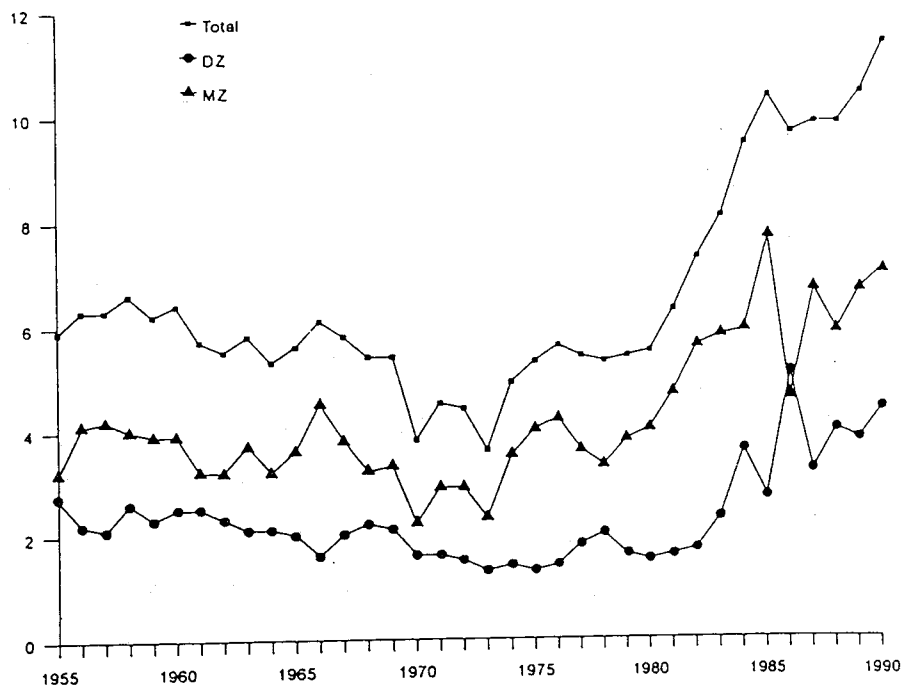在產科學、流行病學、護理學或社會經濟學上，多胞胎妊娠尚有許多有待探討的地方，我們期待有更多人來參與這方面的研究。

Fig. 1 Secular trend of twinning rate in Taiwan from 1955 to 1990.
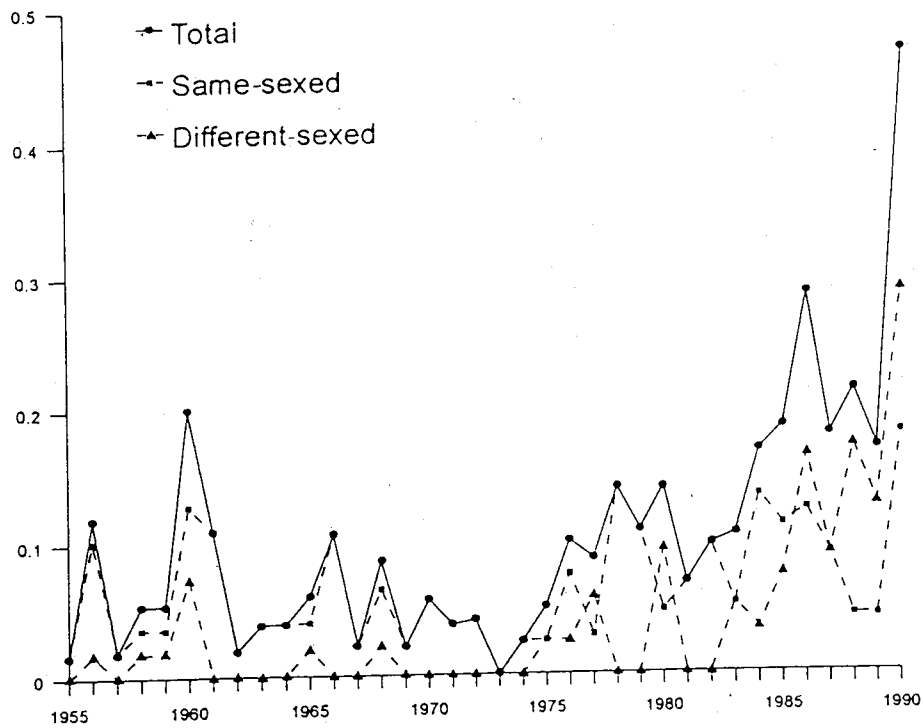
圖 1 台灣 1955 到 1990 年雙胞胎發生率之變遷

Fig. 2 Secular trend of triplet incidence rate in Taiwan from 1955 to 1990.

圖 2 台灣 1955 到 1990 年三胞胎發生率之變遷

表1 近年來台灣多胞胎妊娠的發生率
Table 1.The incidence of multifetal pregnancy in recent years

	NTUH (1991-95)	CGMH (1990-95)	MCMH (1993-95)	Taipei (1985-89)	Total
Delivery No.	11309	24648	11318	73264	120539
Twin					
No.	243	364	415	844	1866
Incidence(%)	2.15	1.48	3.67	1.15	1.55
Triplet					
No.	19	18	30	NA	67
Incidence(%)	0.17	0.07	0.265	NA	0.14
Quadruplet					
No.	2	1	4	NA	7
Incidence(%)	0.018	0.004	0.035	NA	0.015

表2 雙胞胎各配型的百分比以及人工協助生殖技術所致之影響
Table 2. The percentage of Zygosity and the impact of ART

	NTUH		CGMH		Taipei		PTYGH	
Percentage of twins by ART	MZ (%)	DZ (%)	MZ (%)	DZ (%)	MZ (%)	DZ (%)	MZ (%)	DZ (%)
30%	49	51						
15%	61*	39*	60	40				
0%	72	28						
unknown					66	34	56	44

* : from estimation
(PTYGH：省立桃園醫院)

表3 台大醫院與長庚醫院中人工協助生殖技術對多胞胎妊娠發生率之影響
Table 3. The influence of ART in the incidence of multifetal
pregnancy in two hospitals

	NTUH(1991-95)	CGMH(1990-95)	Total
Delilery No.	11309	24648	35957
Twin No.			
Total	243	364	607
Natural	158	309	467(77%)
By ART	70	55	125(21%)
Unknown	15	0	15(2%)
Incidence			
total twin (%)	2.15	1.48	1.69
natural twin (%)	1.41	1.26	1.30
			(1/77)
Triplet No.			
Total	19	18	37
Natural	0	7	7(19%)
By ART	19	11	30(81%)
Incidence			
total triplet (%)	0.17	0.073	0.103
natural triplet (%)	0	0.028	0.019
			(1/5263)

表4 胎次與母親年齡對同卵雙胞胎與異卵雙胞胎的影響
Table 4. Multiple logistic regression analysis of MZ and DZ twinning
by parity and maternal age

Variable	Group	Odds ratio	
		MZ	DZ
Maternal age	<25	1.0	1.0
	25-29	0.6	1.0
	30-34	0.5	0.8
	35+	0.3	0.3
Parity	1	1.0	1.0
	2	2.6	2.3
	3	6.0	5.3
	4+	31.9	22.6

表5 雙胞胎之性別差異
Table 5. The sex ratio in the twins

	Male	Female	M-F Ratio
Singleton			
Hsieh TT 1991	24,120	22,410	1.08
USA 1987			1.05
Twin			
Hsieh TT 1992	671	651	1.03
USA 1987			1.01
Teng RJ 1994	352	380	0.93

表6 美國白人生產之性別比率
Table 6. Sex proportion (% males & female) and sex ratio in US
white births (1933-48)

	Male(%)	Female(%)	M-F ratio
Singletons	51.59	48.41	1.07
Twins	50.85	49.15	1.03
Triplets	49.54	50.46	0.98
Quadruplets	46.48	53.52	0.87

表7 EFPTS依配型與胎盤型式不同之性別比率
Table 7. Sex proportion (% males & female) and sex ratio in the EFPTS according to
zygosity and placentation (2811 pairs)

	Male(%)	Female(%)	M-F ratio
Dizygotic	51.8	48.2	1.07
Monozygotic	48.7	51.3	0.95
DC	49.3	50.7	0.97
MC-DA	49.3	50.7	0.97
MC-MA	23.1	76.9	0.30

表8 台大醫院與長庚醫院中經人工協同生殖技術後三胞胎之性別比率
Table 8. Sex ratio in triplets from NTUH and CGMH conceived by ART

	Male	Female	M-F ratio
NTUH	29	22	1.32
CGMH	18	15	1.20
Total	47	37	1.27

表9 不同方式受孕之雙胞胎之性別比率
Table 9. Comparison of sex ratio in twins between different methods
of conception

	NTUH(1991-95)			CGMH(1990-95)			Total	
	M	F	M/F	M	F	M/F	M/F ratio	
C.C. or HMG	27	19	1.42	14	10	1.40	41/29	(1.41)
AIH or AID	16	14	1.14	12	4	3.00	28/18	(1.56)
GIFT				12	6	2.00	12/ 6	(2.00)
IVF	31	33	0.94	12	22	0.55	43/55	(0.78)
Total	74	66	1.12	50	42	1.19	124/108	(1.15)

表10 台北市多胞胎妊娠之周產期預後

Table 10. Compiled perinatal outcome of the multifetal pregnancies in Taipei

	Singleton	Twin	Triplet
Gestational age (weeks)	39.2±3.0	36.5±2.9	32.6±8.9
Preterm labor	5.6%	36.9%	75%
Birth weight (gm)	3,256±388	2,432±543	1,689±483
Low birth weight (<2,500 gm)	5.9%	47.9%	79.6%
RDS	0.97%*	7.7%	20.0%
NEC	0.054%*	0.7%	4.4%
IVH		1.8%	11.1%
PDA		3.9%	8.8%
Perinatal mortality	0.7%	5.4%	12.1%

*: from estimation

表11 不同研究中三胞胎妊娠之結果

Table 11. Natural course of triplets in different series (*)

	Number (sets)	Mean week at delivery	Delivery weeks(%)			Perinatal mortality(/1000)
			<37	<32	<28	
Australian IVF	32	---	97	39	3	---
Newman et al	198	34	88	20	7	50
Lipitz et al	78	33	86	26	10	93
Gonen et al	24	32	100	---	---	69
Itzkowic	59	33	83	25	10	273
Syrop and Varner	20	33	75	---	15	216
NTUH+CGMH	37	33	78	30	19	121
Total	448	33	87	29	10	105

*: Periods of study:
  Australian IVF, 1979-85
  Newman et al, 1985-88
  Lipitz et al , 1975-88
  Gonen et al, 1978-88
  Itzkowic, 1946-76
  Syrop and Varner, 1946-83
  NTUH+CGMH, 1990-95

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