中華民國周產期醫學會
1993年度報告
臺灣先天性畸型之現狀

Society of Perinatology, R.O.C.

1993 Annual Report

Congenital Malformation in Taiwan: Background, Prenatal Diagnosis, Postnatal Management

中華民國周產期醫學會

1993年11月編印

The Society of Perinatology, R.O.C.

November, 1993

Foreword

Perinatal medicine is the discipline of medicine which concerns the pregnant women, fetuses and newborns. With the recent progress in perinatal medicine, many diseases can now be diagnosed *in utero*. This has completely changed disease patterns in the pediatric population. Furthermore, adult diseases may also be predicted in the early stages of life. Notable examples are cystic fibrosis and Huntington's disease. In the future, chronic diseases such as diabetes mellitus, hypertension, coronary heart disease and even cancer may be predicted in the beginning of life. Thus, preventive measures can be instituted.

Congenital malformation has become the number one cause of neonatal and infant death in Taiwan. It is also the major cause of long-term disabilities. Since 1984, there has been a national effort to curb congenital malformation in Taiwan under the auspices of the National Health Administration. Noticeable changes have been a result of this effort, namely the establishment of an amniocentesis service and a neonatal screening program. Recently, the Society of Perinatology of the ROC has been endorsed by the National Health Administration to establish a maternal serum screening program for Down Syndrome through collaborative efforts of major medical centers. This program is expected to be completed in three to five years. With these efforts, Taiwan will become the first Asian country with such a wide spectrum of prenatal care for congenital malformations.

In the battle against congenital malformation concerted efforts are necessary. A hands-on approach is required to execute the policies of the National Health Administration. The Society of Perinatology of the ROC, which has an array of experts involved in taking care of mothers, fetuses and newborns, undoubtedly has the ability, support and obligation to contribute to this campaign against congenital malfomation.

In the annual report of 1993, we summarized the background, prenatal diagnosis and postnatal management of congenital malformation in Taiwan in order to determine what measures need to be taken in the future and to serve as a reference for our Health Authority during the process of policy-making.

In the coming years, the Society of Perinatology of the ROC will issue an annual report focusing on important issues of perinatal care in Taiwan. In the dawn of national health insurance, we must plan carefully to provide the very best perinatal care to our mothers, fetuses and newborns. This is undoubtedly an important indicator of the extent of development in our country. The Society of Perinatology of the ROC takes an oath to devote itself fully to this goal.

We are in debt to Dr. T'sang T'ang Hsieh, Secretary General of our society, who has greatly contributed to the preparation of SPROC's annual report

Fon-Jou Hsieh.M.D.
President,
Society of Perinatology of the ROC
November, 1993

CONGENITAL MALFORMATION IN TAIWAN: BACKGROUND, PRENATAL DIAGNOSIS AND POSTNATAL MANAGEMENT

Introduction

Thanks to advances in antibiotic treatment, nutrition, and improved neonatal management, neonatal deaths have fallen sharply over the last 30 years. Currently in Taiwan, congenital anomalies account for an increasing proportion of neonatal deaths.

For instance, during the 1960s the leading cause of neonatal death was premature delivery (50%); in the 1990s, however, congenital anomalies account for about one-third of all neonatal deaths (31%) (Table1). Similarly, during the 1960s, premature delivery was the leading cause of infant mortality (25%); whereas today, congenital anomalies have become the principal cause of infant death (30%)(Table 2).

In fact, in spite of continuing progress in the prenatal detection of congenital anomalies, the majority of congenital malformations remain undiagnosed until after birth. Physicians, patients, and society therefore all face the tremendous responsibility of providing a decent life for these handicapped individuals.

Incidence

The annual number of births in Taiwan ranged from a high in 1984 of 396 725, to a low in 1986 of 308 187, with an average of 330 000 (Figure 1) . With an incidence of 1. 4%, there are at least 4 500 children born with congenital anomalies each year (Table 3). Unfortunately, a large portion go undiagnosed until after birth.

This condition has become an important issue for both society and the government . Thus, in 1986 the Department of Health established a voluntary congenital malformation surveillance registration system. During the period from 1986 to 1992, only one-tenth of all deliveries were registered, although this year the registration system will expand to include one-half of all deliveries, and will eventually include all newborns (Figure 2) . Thus far, the exceptions have been private clinics and countryside hospitals. Nevertheless, even among the deliveries registered, we strongly suspect there remains some underreporting.

We used several databases in Taiwan, including those of the National Taiwan University Hospital[1], Kaohsiung Medical College Hospital[2], Chang Gung Memorial Hospital, and the registry of the Department of Health. Using this information, we found the incidence of anomalies of the central nervous system to be 2.09/1000 births; of the cardiovascular system to be 0.93/1000 births ;of the gastrointestinal system to be 0.70/1000 births;of the genitourinary system to be 0.82/ 1000 births; of the musculoskeletal system to be 2.07/1000 births; of craniofacial defects to be 1.80/1000 births; and of chromosomal abberation to be 1.59/1000 births. The most prevalent anomalies of the central nervous system are anencephaly and hydrocephaly. The incidence of anencephaly is about 1/1000 births. For the gastrointestinal system, the major anomaly is imperforated anus, averaging about 0.26/1000 births. Gastroschisis (0.21/1000), omphalocele (0.16/1000), and diaphragmatic hernia (0.20/1000) are all surgically correctable anomalies. If diagnosed prenatally, physicians can be prepared for postnatal correction, thereby raising the survival rate (Table 4)[3]. Cleft lip with or without cleft palate occurs in about 1.7/1000 births; distal anomalies, including polydac-

tyly, are the major problems associated with the musculoskeletal system, averaging about 1.4/1000 births (Table 5-10).

Prenatal Diagnosis

Cytogenetic disorders

The government also has a subsidiary system to encourage mothers at high risk of chromosomal anomaly to undergo genetic amniocentesis. One third of the fee for amniocentesis is paid by the government.

This governmental financial support has helped to more than triple the number of mothers 34 years or older receiving amniocentesis: from an initial 7.7% in 1987, the figure has risen steadily to a current high of 17.1% in 1990. Still, the Department of Health hopes eventually to increase the rate to over 30% (Table 11).

The indications for amniocentesis for cytogenetic study are as follows: advanced maternal age ,65.2%; previous chromosomal aberrations, 6%; a family history of chromosoal anomaly, 2.4%; previous fetal anomaly, 7%; intrauterine abnormality, 5%; and others, 17.7%[4,5].

The results of genetic amniocentesis show, however, only an average abnormality rate of 2.62% (Table 12). Among these anomalies, 57.4% are numeric and 42.6% are structural. Trisomy 21 accounts for 22% of the all abnormalities (Table 13)[4].

Among postnatal chromosomal anomalies, one-third are Down syndrome. This means, in Taiwan, one in every 800 children born is a Down syndrome baby (Table 14); a mere 13% are diagnosed prenatally. This puts a large burden on us as doctors to develop additional methods of prenatal detection, and on the government to promote and assist in postnatal management.

Although now in our prenatal diagnosis of chromosomal anomalies we focus on women 34 and older, they account for only 15% of all Down babies. Yet, when correlated against their percentage of the delivery population, women 30 years and older are in fact 2.5 times more likely to be carrying a Down syndrome baby than women under 30 (Figure 3). Therefore, we must emphasize additional methods of early detection, such as alpha-fetoprotein (AFP) screening.

Alpha-fetoprotein screening

In recent years, AFP screening has become popular in Taiwan as an additional tool for early in utero detection of neural tube defects and chromosomal anomalies[6]. Results at Chang Gung Memorial Hospital using this technique have, however, been disappointing.

From December 1988 through March 1990, a total of 4040 women received AFP screening during their 15th to 20th week of gestation. Among these, 87 subsequently underwent amniocentesis due to their low AFP level. One case of Down syndrome was diagnosed. In other words, we performed over 4000 screenings to detect one case of Down syndrome.

The detection rate can, nevertheless, be raised by coupling AFP screening with maternal serum human chorionic gonadotropin (hCG) screening[7]. Unfortunately, the hCG screening program is only in its preliminary stage of development. The results are encouraging: under retrospective review of the Down syndrome cases, four out of five fall beyond 2.5 of the multiple of the median.

Another important way to increase the yield of amniocentesis is to screen abnormal fetuses by ultrasound. This increases the yield to almost 20%[8-15].

Chorionic villus sampling

Chorionic villus sampling (CVS) has become an important technique in prenatal genetic diagnosis. Although originally believed by doctors to be a fairly safe procedure[5], reports of limb defects after CVS since 1991 have raised great concern over its safety[16].

To clarify the causal relationship between the two--CVS and limb defects--a survey of limb defects naturally occurring and after CVS was conducted by questionnaire in Taiwan in 1991. From 78 752 deliveries and 1362 CVS cases surveyed, the incidence of limb defects was found to have increased

(natural: 25/78 742 vs. after CVS: 3/1362: P<0.001), and the defects occurring after CVS were found to be far more severe than those occurring naturally. Since many of the CVS performed in Taiwan are for determining sex, the incidence of limb defects after CVS may have to be doubled, to probably around 0.1-0.2%. Inexperience and early and multiple CVS will increase the incidence and severity of the defects. Thus, detailed screening at 20 weeks of every fetus for which CVS has been performed should be strictly observed.

Cordocentesis

Percutaneous fetal blood sampling (cordocentesis) offers invaluable information on fetal physiology and fetal disease. This technique was introduced to Taiwan in 1985 and has become an important tool in prenatal diagnosis[17]. The fetal loss rate due to the procedure is only 1%[18]. It not only makes diagnosis of various fetal diseases possible (Table 15), but it also has important therapeutic implications, as demonstrated by intravascular transfusions and therapeutic agent injections[19].

Thalassemia

Thalassemia is widespread throughout Southeast Asia. Currently in Taiwan, 4.5% of the population are alpha-thalassemia carriers and 1.5% are beta carriers[20,21]. If both husband and wife have the same type of thalassemia, the baby is at a high risk of homozygous thalassemia, which results in severe anemia requiring blood transfusions, and may even result in fetal death. Thus, thalassemia is another important problem calling for early detection.

The Department of Health has a screening program for thalassemia (Figure 4). Every pregnant woman receives a complete blood count. If her mean corpuscular volume is less than 80, or mean corpuscular hemoglobin is less than 25, her husband will be checked for complete blood count. Should his results be the same as those of his spouse, both must receive further examinations, among them tests for iron deficiency anemia.

These tests may be performed by any obstetrician. If, however, husband and wife both register abnormal, the doctor must send blood samples to a medical center for DNA diagnosis. In the event both are the same type of carrier, the mother will receive CVS, amniocentesis, or cordocentesis for fetal diagnosis (Figure 4). There is a one in four chance their baby will have a severe form of anemia.

Environmental teratogens

Environmental influences have been postulated as an important contributing factor to human malformation. This is particularly noteworthy due to the increasing pollution resulting from years of industrialization in Taiwan. Two notable examples are thalidomide embryopathy and polychlorinated biphenyls(PCBs) intoxication.

Out of 315 children with congenital malformations born since 1958, 38 have been diagnosed as caused by thalidomide. Among these were: one case of amelia, four of phocomelia, 15 of oligodactylia with a radial defect, five instances of an additional thumb, two cases of triphalangism of the thumb and 10 cases of ear deformities. The import and sale of thalidomide was banned in 1962[22].

In 1978, contamination of oil with PCBs resulted in widespread intoxication in central Taiwan--the so-called "oil disease". Children prenatally exposed to heat-degraded PCBs were born with intrauterine growth retardation, discolored skin, and skin eruptions. According to a recent study, those children prenatally exposed have shown poorer cognitive development than their controls. The discrepancy continued up to the age of 7, and even children born long after the exposure were still affected[23].

Virus infection is also a significant teratogen in Taiwan. "In utero" infections of rubella, varicella, and cytomegalovirus are possible causes of congenital malformations.

Only 50-80% of the women of reproductive age have protective rubella antibody. Instead of an epidemic once every 10 years, as in the old days, rubella is now undergoing a

small resurgence in Taiwan. Each year, especially during the spring, outbreaks of rubella have been noted. These outbreaks are a threat to pregnant women lacking the rubella antibody. Eradication of rubella outbreaks by immunizing adolescent girls is being pushed by health authorities. but it will take years to achieve this goal. Varicella is also a frequent viral infection among young children. It has been estimated that at least 10% of the women of reproductive age lack protective antibodies. This highly infectious disease poses a real threat to pregnant women, causing congenital varicella syndrome. Screening for varicella antibody and immunization should be considered. Cytomegalovirus can also cause severe sequelae in the infected fetus. However, there is no way of protecting pregnant women from this devastating infection. Perhaps sophisticated prenatal diagnoses may help to detect some infected fetuses.

Sonographic Diagnosis

Thanks to advances in sonographic technology, nearly every practicing obstetrician in Taiwan has an ultrasound machine in their office. Over the years, the number of members in the Society of Ultrasound in Medicine, ROC, has grown steadily. Presently, this society numbers almost 4 000 members. Of these, the vast majority, over one quarter, are obstetricians (Figure 5).

Further, the society offers both basic and advanced training courses for members. As the expertise in sonographic diagnosis rises, the number of congenital anomalies diagnosed prenatally will rise with it.

We now strongly advocate detailed ultrasound screening of every fetus at 20-22 weeks. Every fetus should be carefully examined by an experienced sonographer and every major organ system including brain, face, heart, abdominal organs, and limbs should be carefully viewed. Also if fetal biometry, including biparietal diameter, abdomen circumference, and femur length, is performed, this approach will facilitate early detection of many fetal disorders. If any anomalies occur, there is ample time for further work, such as cytogenetic study, to determine the proper method of managing the fetal condition.

Many congenital heart diseases (CHD) can now be diagnosed prenatally. The importance of this procedure is clear: one in every 200 babies is born with some form of CHD. Furthermore, CHD may cause antepartum fetal problems, such as heart failure and hydrops. Also, a high percentage of cases of CHD are associated with chromosomal anomalies. If we can detect CHD before delivery, it will help us with the subsequent neonatal management.

At Chang Gung Memorial Hospital from March 1990 through April 1993, we screened a high risk group for CHD. This group included mothers with a history of CHD, maternal conditions (such as diabetes), advanced maternal age, exposure to teratogens, and multiple gestation. From 1282 cases, 49 cases of congenital cardiovascular malformation and 62 cases of arrhythmia were detected. As seen from the figures in Table 16-17: eight instances of endocardiac cushion defect, four cases of tetralogy of Fallot and three of Ebstein's anomaly were detected prenatally.

Fetal Management

Treating fetal diseases in utero is the most logical approach. Good results in treating Rh isoimmunization by intrauterine transfusion and fetal arrhythmia by antiarrhythmic drugs have been achieved. However, in utero correction of fetal structural problems are far from ideal. Only bilateral urinary tract obstruction, obstructive hydrocephalus, and congenital diaphragmatic hernia are thought to require mandatory intrauterine correction. Still, the outcome of treated fetuses is very poor. So, the mainstays of fetal management are termination and postnatal correction.

Medical treatment of fetal arrhythmia

Supraventricular tachycardia including paroxysmal supraventricular tachycardia, atrial flutter, and nodal tachycardia have all been treated successfully in Taiwan[24]. Cordocentesis offers direct access to the fetal cir-

culation and renders delivery of therapeutic agents, like blood components or antiarrhythmic drugs, possible.

Intrauterine management

Intrauterine therapy has its limitations. In fact, the term infant is a better anesthetic and surgical risk than the preterm infant. Furthermore, management in utero also puts the mother at risk. Hence, at present, only a few conditions are handled before birth, such as bilateral urinary tract obstruction, obstructive hydrocephalus, and congenital diaphragmatic hernia. Consequently, termination and postnatal correction are the mainstays of fetal management[9,12] ;fetal therapy is done only in highly selective cases. For instance, postnatal correction of omphalocele and gastroschisis boasts a 71% and 85% survival rate, respectively (Table 4)[3].

Termination

Termination is a unique option of handling fetal disease. With timely prenatal examination, single gene disorders can be found by CVS at 9-10 weeks, and the affected fetus can be terminated safely and simply by therapeutic dilatation and curettage.

However, fetal disorders detected by midtrimester genetic amniocentesis and ultrasound screening are preferably terminated by induction of labor (which is much safer than dilation and evacuation) once the fetal abnormality has been deemed incompatible with life. Furthermore, the availability of various prostaglandin preparations like PGE2 has greatly facilitated the successful evacuation of intrauterine contents[25].

However, fetal diagnosis should be ascertained before 24 weeks, a line drawn by our law. After that, the fetus is considered able to live "extrauterinely" and termination is not a proper option beyond this fixed limit.

Postnatal Management

Newborn screening

We now do a good job of screening for neonatal metabolic diseases. In 1991, almost 90% of all newborns were screened (Table 18). The most frequent problem encountered in Taiwan is glucose-6-phosphatase deficiency (G6PD), followed by congenital hypothyroidism (CHT) and phenylketonuria (PKU)(Table 19).

The incidence of G6PD in females is 1/111, and in males 1/34, followed by CHT (1/3 102), and PKU (1/51 880): galactosemia (GAL) and homocystinuria (HCU) are rarely encountered (Table 20)

Social support

If unfortunately a Down baby is not diagnosed prenatally, 76% are detected within the first month, due to the unique appearance of the infant.

For a couple raising a Down syndrome baby, the financial burden is daunting. Since 31% of all Down syndrome cases have associated congenital heart disease[26], the resulting medical costs alone average NT$3 000 per month. Coupled with the special education expenses, caretaking fees, and so on, the average family's monthly outlay is NT$25 000. (The per capita monthly income is currently NT$20 000; in other words, for a husband and wife, their Down syndrome child takes more than half of their income.)

To help relieve this tremendous burden, roughly two-thirds turn to private foundations. Another 13% or so enroll their children in special education programs, and another 6% are forced to place their child in a medical unit. Social welfare unfortunately accounts for only 5.4% of the assistance to these families.

The annual income per capita in Taiwan has reached US$10 000. Only six countries in Asia have achieved this level of affluence. However, almost no social resources have been allocated to the care of handicapped children. With this tremendous burden, no wonder many handicapped fetuses or newborns are given up by their parents. Taiwan really is a "rich but greedy" country.

Surgical correction

With advances in surgical technique, anesthesia support, and total parenteral nutrition, a good outcome can be achieved with pediatric surgery. Furthermore, prenatal diagnosis also facilitates surgical management of the fetus. For example, the establishment of a diagnosis prenatally greatly improves the outcome of meconium peritonitis and abdominal wall defects. As reported by Hsieh et al. in conjunction with prenatal diagnosis, surgical correction of a wide range of fetal structural disorders including th gastrointestinal and genito-urinary systems has achieved a rather acceptable outcome[12,27]

The first successful separation of ischiopagus conjoined twins was done on September 10, 1979 at the National Taiwan University Hospital. Since then, totally nine pairs of conjoined twins with different extents of conjoining have been separated at the National Taiwan University Hospital. However, the birth of conjoined twins is the greatest failure of obstetricians in this era of prenatal diagnosis.

Another problem facing obstetricians in Taiwan is craniofacial defects, which occur at a rate of two cases in 1000 births, cleft lips and/or cleft palates alone occur in 1/500 to 1/600 births. This kind of anomaly causes feeding problems, and later, speech and cosmetic difficulties. Cosmetically, these defects may have a deep influence upon a child's personality. Thus craniofacial malformation is a big issue in postnatal management.

As the defect is not incompatible with life, the fetus should not be terminated after diagnosis. Instead, after the baby is born, the parents should seek medical help. However, many parents still terminate a pregnancy when a cleft lip or palate is diagnosed in utero, even beyond the 24th week.

Fortunately, Dr. Nordhoff, chief of the Craniofacial Center of the Chang Gung Memorial Hospital, has set up the Nordhoff Craniofacial Foundation to help these children. However, it must be emphasized that with this sort of deformity, the patient needs a team of experts: not only corrective surgeons, but also social workers, speech pathologists, and clinical psychologists are needed. The cost, however, is high; cosmetic surgery alone hovers around NT$100 000.

In addition to the Down syndrome and craniofacial foundations, Taiwan also has a Congenital Heart Disease Foundation to help with the medical care of children with congenital heart diseases.

Although Taiwan is now rich, social welfare is still poor. Therefore, those concerned about these problems should contribute their money and time to help these disadvantaged children lead normal lives.

Summary

It is our belief that every child has the right to be born "normal". Although "normal" is not easy to define, we can define "normal" as without significant handicap. To achieve this goal requires a concerted effort from everyone in society.

Firstly, public awareness and participation is of the utmost importance. Screening of every couple in the preconceptional stage and then a complete prenatal diagnosis workup for every pregnancy should be strictly reinforced. Improvements in the field of prenatal diagnosis, neonatology, and neonatal surgery are also of vital importance. In view of the extremely unbalanced distribution of medical resources on the island, establishment of a network for prenatal care in the central, southern, and eastern parts of Taiwan should be started without delay.

Acknowledgments

Authors would especially like to thank the Bureau of Health Promotion & Protection, Department of Health, the Executive Yuan, Dr. Man-Li Yang of Veterans General Hospital, Dr. Shio-Jen Lin of Cheng Kung University and Dr. Mei-Chyn Chao of Kaohsiung Medical College for very kindly supplying some of the information used in this article.

References

1. Shyu MK, Ko TM, Lee CN, et al. Congenital anomalies at the National Taiwan University Hospital in the past 22 years : analysis of 55 339 deliveries. Adv Obstet Perinatol 1992; **3**:14-8.
2. Chao MC: Congenital malformations in Kaohsiung Medical College Hospital (1979-1988): a need for genetic counseling. Acta Paed Sin 1985; **26**:375.
3. Chang PY, Yeh ML, Sheu JC, Chen CC. Experience with treatment of gastroschisis and omphalocele. J Formosan Med Assoc 1992; **91**:447-51.
4. Hsieh FJ, Ko TM, Tseng LH, et al. Prenatal cytogenetic diagnosis in amniocentesis. J FormosanMed Assoc 1992; **91**:276-82.
5. Hsieh TT, Lee JD, Kuo DM, et al. Perinatal outcome of chorionic villus sampling versus amniocentesis. J Formosan Med Assoc 1989; **88**:894-9.
6. Ko TM, Hsieh FJ, Wu CC, et al. The significance of abnormally high and low maternal serum alpha-fetoprotein levels between 14 and 25 weeks of gestation. J Formosan Med Assoc 1990; **89**:456-60.
7. White I, Papiha SS, Magnay D. Improving methods of screening for Down's syndrome. N Engl J Med 1989;**320**:401-4.
8. Hsieh FJ, Lee CN, Wu CC, et al. Antenatal ultrasonic findings of craniofacial malformations. J Formosan Med Assoc 1991; **90**:551-4.
9. Hsieh FJ, Jou HJ, Ko TM, Chen HY. Sonography of the fetuses with chromosomal aberrations. Adv Obstet Perinatol 1991; **2**:29-35.
10. Hsieh FJ, Chen SU, Chang FM, et al. Prenatal sonographic diagnosis and proper management of congenital gastrointestinal obstruction: report of 5 cases. J Formosan Med Assoc 1988; **87**:484-9.
11. Chen HY, Hsieh FJ, Huang LH. Prenatal diagnosis of conjoined twins by real-time sonography: a case report. J Clin Ultrasound 1983; **11**:94-6.
12. Hsieh FJ, Chang DY, Chen HY, Huang LH, Lu CC, Huang DS. Antenatal diagnosis of conjoined twins. J Formosan Med Assoc 1988; **87**:393-7.
13. Hsieh FJ, Lun CR, Chen WJ, Chen CC, Tsai TC. Prenatal diagnosis and postnatal management of surgically correctable fetal malformations. J Formosan Med Assoc 1989; **88**:226-31.
14. Liu JY, Lee SK. Antenatal sonographic diagnosis of thanatophoric dwarfism: a case report. J Obstet Gynecol ROC 1984; **23**: 237-42.
15. Hsu JJ, Chiu CH. Ultrasound finding in polycystic kidney: a case report. J Ultrasound Med ROC 1991; **8**;322.
16. Mastroiacavo P, Cavalcanti DP. Limb-reduction defects and chorion villus sampling. Lancet 1991; **337**:1091.
17. Hsieh FJ, Chang FM, Ko TM, Chen HY. Percutaneous ultrasound-guided fetal blood sampling in the management of nonimmune hydrops fetalis. Am J Obstet Gynecol 1987; **157**:44-9.
18. Hsieh FJ, Ko TM, Chang FM, Chen HY, Kao ML, Furng MH. Percutaneous ultrasound-guided fetal blood sampling: experience in the first 100 cases. J Formosan Med Assoc 1989; **88**:137-42.
19. Hsieh TT, Kuo DM, Lo LM. Successful treatment of idiopathic hydrops fetalis by albumin injection through cordocentesis. J Obstet Gynecol ROC 1990; **29**:142-4.
20. Ko TM, Ko PM, Chen CJ, Hsieh FJ, Hsieh CY, Lee TY. Incidence study of heterozygous thalassemia in northern Taiwan. J Formosan Med Assoc 1989; **88**:678-81.
21. Ko TM, Hsieh FJ, Chen CJ, Hsu PM, Lee TY. Cord blood screening for alpha-thalassemia in northern Taiwan.J Formosan Med Assoc 1988; **87**:146-9.
22. Yang TS, Chang-Shen CC, Wang CM. Survey of thalidomide embryopathy in Taiwn. J Formosan Med Assoc 1977; **76**;546-62.
23. Chen Joseph YC, Guo YL, Hsu CC, Rogan WJ. Cognitive development of Yu-Cheng ('Oil Disease') children prenatally exposed to heat-degraded PCBs. JAMA 1992; **268**:3213-8.
24. Lin YF, Lee CN, Ou JW, Hsieh FJ, Chen HY. Prenatal diagnosis of fetal atrial flutter: a case report. Adv Obstet Perinatol 1992; **3**: 98-101.
25. Lee CN. Clinical trial of intravenous Nalador (PGE2) infusion for second-trimester abortion. Anniversary commemoratory symposium for Professor CT Hsu. May 9, 1993.
26. Lin SJ, Hu SC, Sheu SF, et al. Anthropometric study on Down syndrome in Taiwan. Pediatrics 1991; **32**:158-64.
27. Lin YM, Chang FM, Liu CH, Chen CJ. Prenatal diagnosis of duodenal atresia and rapid surgical correction after birth: a case report. J Perinatol ROC 1990; **1**:33.

台灣先天畸型之背景、產前診斷與產後治療

簡介(Introduction)

由於抗生素的發達，營養的改善，和新生兒醫療服務品質的提高，新生兒的死亡率在過去30年來已降低很多。在台灣地區，先天性畸型已經躍居為新生兒死因的前幾名。

在1960年代，早產兒是造成新生兒死亡的主要原因(佔50%)。在1990年，先天性畸型已經佔新生兒死亡的1/3(約31%)(表一)。相同的，在1960年代，早產兒也是嬰兒死亡率的首要原因(25%)，但是在今天，先天畸型是嬰兒死亡的主因(30%)(表二)。

事實上，雖然產前診斷先天畸型的技巧在目前已有十足的進步，但是大部分的先天畸型仍須延至出生後才能診斷出來，使得醫事人員、病患家屬和社會都必須面對照顧先天缺陷兒的責任和沉重負擔。

發生率(Incidence)

在台灣新生兒的人數已經從1984年的39萬人(396,725)降至1986年的30萬人(308,187)，目前大約維持在每年33萬人左右(圖1)，以1.4%的先天缺陷兒發生率來計劃，每年至少有4,500個先天缺陷兒誕生，不幸的是，大部份的個案，都要延至出生後才能診斷出來。

預防(Prevention)

這種情形已成為社會和政府的重要課題，因此在1986年，衛生署保健處建立了一種「先天性缺陷兒的登錄系統」，然而從1986年至1992年，只有1/10的生產已經登錄，在這一兩年將擴充至1/2的生產，最終希望能未到100%生產登錄的理想(圖2)，這些遺漏登錄的，主要是私人診所或位處偏僻的醫院，即使是有參與登錄的醫院，可能未登錄的先天性缺陷兒也要比有登錄的比例高得多。

利用台大、高醫、長庚3家醫院和衛生署的生產資料庫作為基礎，我們得到以下的結果：先天性缺陷兒在中樞神經系統的發生率為2.09/1000，在心臟血管系統為0.93/1000，在腸胃消化道系統為0.82 /1000，在骨骼肌肉系統為2.07/1000，在頭顏面缺陷為1.8/1000，和染色體異常為1.59 /1000。在中樞神經系統最常見的為無腦兒和水腦症，無腦兒的發生率為10/1000；在腸胃道系統最大發生的的是先天性無肛症，發生率為0.26/1000。其中腹壁裂(gastroschisis,0.21/1000)，臍膨出(omphalocele,0.16 /1000)和先天性橫隔疝氣(diaphragmatic hernia, 0.2 /1000)為手術可以矯正的先天性缺陷，如果在產前可以診斷，醫師可以在胎兒出生後馬上手術矯正，這樣可以提高存活率(表4)。兔唇但是不含併顎裂的發生率為1.7 /1000；四肢末端的異常，包含多指症，發生率約1.4 /1000，是為最常發生的骨骼肌肉系統異常。

產前診斷(Prenatal diagnosis)

染色體異常(cytogenetic disorders)

政府建立一個系統來鼓勵高危險群孕婦接受羊水穿刺，並且實際以政府經費來補助1/3的羊水費用。政府的補助，使得高齡孕婦接受羊水穿刺的比例由1987年的7.7%,增加至1990年17.1%，經由衛生署的大力鼓吹，希望將來能把接受率提高至30%(表11)。

常見接受羊水穿刺的適應當為：1.高齡孕婦(65.2%)2.曾育有染色體異常的小孩(6%)3.家族中曾育有染色體異常的小孩(2.4%)4.曾育有先天性異常胎兒(7%)5.超音波發現胎兒異常(5%)6.其他原因(17.7%)。但是羊水穿刺後，發現染色體異常的比例不高，平均而言，只有2.62%(表12)。這些染色體異常，有57.4%為染色體數目異常，42.6%為染色體構造異常，唐氏症(trisomy 21)約佔所有染色體異常中的22%(表13)。

至於新生兒的染色體異常，1/3為唐氏症，也就是說，以台灣唐氏症的發生率為1/800來計算，只有13%的唐氏症，在產前就被診斷出來(表14)，因此婦產科醫師必須花費相當大的心力，找出其他方法來產前診斷唐氏症。

雖然我們把大部分的注意力集中在34歲以上的高齡孕婦，力勸她們做產前診斷，事實上這些高齡孕婦會誕生的唐氏症，只佔全部唐氏症新生兒的15%。當然經過更精確的統計，這些高齡產婦懷有唐氏症的機率，還是比一般30歲以下的孕婦要高出2.5倍。這樣的事實，使得我們必須再合併使用其他的方法，來提高產前檢替唐氏症的比例，篩檢母血中甲型胎兒蛋白的系統就被發展出來了。

甲型胎兒蛋白篩檢(Alpha-feto protein screening)

近幾年來，台灣已經開始引用甲型胎兒蛋白篩檢的系統來作為產前診斷神經管缺損及染色體異常的輔助工具，可惜的是，這種篩檢的成效，在長庚醫院的數千例經驗中，令人感到失望。

從1988年12月至1990年3月，在長庚醫院共有4040位懷孕15至20週的孕婦接受甲型胎兒蛋白的篩檢。結果共有87位孕婦的甲型胎兒蛋白的值偏低，需接受進一步的羊水穿刺確認。只有1位唐氏症因此而被診斷出來，也就是說，我們篩檢了4000側孕婦的甲型胎兒蛋白，結果只找到1個唐氏症胎兒。

當然如果能合併人類絨毛性腺激素(hCG)作篩檢，那麼篩檢率將提高許多。可惜這部份的檢查，仍然只是在初步發展的階段。因此我們回溯以前的個案，發現5例唐氏症中有4例的人類絨毛性腺激素高出中位值的2.5倍，另外一個可以提高羊水穿刺診斷率的方法為超音波，利用超音波找出構造異常的胎兒，可以使得偵測率增加至20%。

絨毛採樣(chorionic villus sampling)

絨毛採樣是產前診斷的一種重要工具，雖然在早期這種檢查被當成一種安全的方法，但是自1991年後，開始有作完絨毛採樣後發生胎兒四肢缺損的報告，因此它的安全性受到嚴重的關切。

為了釐清絨毛採樣和四肢缺損之間的關係，1991年在台灣進行大規模的問卷調查，共統計了78752位新生兒和1362位接受絨毛採樣的個案，結果發現作過絨毛採樣後發生肢體缺損的比例遠比一般未作過絨毛採樣者為高　(3/1362：25/78742)，而且發生肢體缺損的嚴重度也比未作絨毛者為高。在台灣，大部分接受絨毛採樣的個案都是為了胎兒性別的鑑定，也就是說，發生絨毛採樣後肢體缺損的個案比例，應該是現有的2倍，大約為0.1－0.2%，可能造成的理由則為醫師經驗不足，或太早期，多次之絨毛採樣，都會增加發生的比例或缺損的嚴重度。因此，做完絨毛採樣的孕婦，在懷孕20週時，一定要仔細用超音波來觀察胎兒的四肢是否健全。

臍血採樣術(cordocentesis)

臍血採樣術自1985年引進台灣醫界後，提供了許多有關胎兒生理及先天性疾病的重要訊息，已經成為臨床診斷的重要工具。這種檢查方法流產率僅有1%，而且臍血採樣術不只可以作為診斷的好幫手，也可以應用於子宮內治療，例如子宮內胎兒輸血，子宮內胎兒治療藥物的注射等。

地中海型貧血(Thalassemia)

地中海型貧血症好發於亞洲的東南地區，台灣也是好發的地區，在台灣有4.5%的人口為甲型地中海型貧血的帶原者，1.5%的人口為乙型地中海型貧血的帶原者。夫妻如果為同型的地中海型貧血的帶原者，所孕有的子女有1/4的機會成為重型地中海型貧血的患者，胎兒會有胎死腹中，或者需終身輸血的情形發生。因此，在台灣早期診斷重型地中海型貧血的胎兒是非常重要的臨床課題。

衛生署已經擬定了一套完整的地中海型貧血篩檢的網路系統(圖4)，每名孕婦在產前檢查的時候，都會做全血球計數檢查(CBC)，如果孕婦本人的平均紅血球體積(MCV)小於80，或者平均血色素的濃度(MCH)小於25，就須要檢查先生的血球，如果夫妻2人的平均紅血球的體積都小，就須要進一步作地中海型貧血的基因確認診斷。

這些全血球計數(CBC)的檢查十分簡單，每一位婦產科醫師都可以在自己的診所完成這些檢查，但是如果夫妻2人的平均紅血球的體積都小的話，醫師就可以直接將夫妻兩人的血液抽好，郵寄到有做基因診斷的醫學中心去做地中海型貧血基因的確認診斷，如果夫妻雙方經診斷為同型的帶因者，所生下的胎兒有1／4的機會為重型患者，孕婦就須要接受絨毛採樣，羊水穿刺或臍血採集術來作胎兒診斷(圖4)。

環境致畸因素(environmental teratogens)

環境因素也是造成畸型的主因之一，尤其在台灣由於工業的發展，各項污染日增，更顯出環境因素的重要，其中最著名要數沙利竇邁(Thalidomide)引起的四肢短小和多氯聯苯(polychlorinated biphenyls, PCBs)引起的傷害。

自1958年以來，在315個先天畸型兒中，有38個被診斷為由沙利竇邁所引起的，包括有

各種四肢末端的異常，因此在1962年沙利竇邁已被禁止使用。

在1978年由於油中含有過量的多氯聯苯(PCBs)，引起中台灣地區一連串的後遺症，因此又稱黑油病“oil disease”，幼兒在子宮內若暴露在過量的多氯聯苯，會導致子宮內生長遲滯，皮膚病變等而且出生後仍會持續有症狀出現，即使在孕婦暴露多氯聯苯後一段時間才誕生的嬰兒，仍然會受到影響。

另一項在台灣會引起畸型的病因為病毒感染，子宮內感染各種病毒，如德國麻疹、水痘、巨噬細胞病毒感染等，都會造成胎兒畸型。

在台灣生育年齡的婦女僅有50-80%具有德國麻疹抗體。以前德國麻疹為每十年一次大流行，但是目前演變為在每年春天左右，有小的流行，沒有抗體孕婦在此時就會受到感染。雖然當衛生當局已在推廣針對青春期的少女打德國麻疹的疫苗，但是這須要數年的時間才能達到全面接種的目的。水痘是幼兒常患的疾病，偏偏育齡的婦女有10%並不具抗體，這些人若感染水痘，往往導致胎兒有先天性水痘症候群(congenital varicella syndrome)，因此在篩檢水痘的抗體並追種苗是值得考慮的。巨噬細胞病毒的子宮內感染，也會造成胎兒的畸型，不過目前並沒無有效的方法可以預防這種疾病的感染，只有依高科技的進步來診斷這種疾病。

超音波診斷(Sonographic diagnosis)

由於超音波技巧的普遍提高純熟，在台灣幾乎每個婦產科診所都有一台超音波。超音波醫學會的人口年年增加，目前已有4000名左右的會員，值得一提的是，有1/4的會員是婦產科醫師(圖5)，由於學會的每年均安排基礎和繼續教育課程，會員操作超音波的技巧日增，使得產前診斷先天畸型的機會也逐年提高。

目前我們建議每個胎兒至少在20-22週左右接受一次詳細的超音波檢查，這項檢查必須由深富超音波經驗的醫師，有系統地詳細檢查重要器官，包括大腦、臉、心臟、腹部器官和四肢；同時要測量胎頭、腹圍和大腿骨的長度以評估胎兒的生長情形，同時可以早期發現胎兒異常。一旦發現超音波異常，往往須要進一步作染色體檢查，作為進一步胎兒處理的重要參考。

有許多先天性的心臟病，現在已能在產前診斷出來，在台灣先天性心臟病發生的比例為200分之1，而且往往會引起胎兒心律不整或水腫等問題，因此亡產前診斷十分重要；而且有相當高比例有先天性心臟病的胎兒，往往併有染色體異常，如果臨床醫師能在產前注意到先天心臟病的問題，就不致於在胎兒出生時手忙腳亂了。

自1990年3月至1993年4月在長庚醫院，共針對高危險群的孕婦做篩檢，這些孕婦包含孕婦本人有先天性心臟病，母親本人有糖尿病，高齡孕婦，曾暴於致癌原和多胞胎懷孕者。由1282個孕婦中，共找出49例先天性心臟血管構造異常和62例心律不整者(表16-17)，其中15例是複雜性的先天性心臟病。

胎兒治療(Fetal management)

在子宮內治療胎兒，理論上是最合邏輯的治療方式。在子宮內針對Rh血型不合的胎兒進行子宮內輸血，和對先天性心律不整的胎兒投以抗心律不整藥物，都有極大的成效。不過

在子宮內手術治療先天性疾病距離理想還有一大段距離。在目前只有兩側泌尿系統阻塞和先天性橫隔疝氣可以在子宮內手術，不過術後的預後仍然不佳，所以目前仍然停留在引產或出生後再予以矯正的階段。

藥物治療胎兒心律不整(medical treatment of fetal arrhythmia)

在台灣，許多胎兒心律不整(如paroxysmal supraventricular tachycardia, atrial flutter, nodal tachycardia)都成功地被產前治療。利用臍血採樣術可以直接監測胎兒血液循環的情形，並直接經由臍帶直接輸血或給予抗心律不整的藥。

子宮內治療(intrauterine management)

子宮內治療有其本身的限制，事實上，足月的胎兒遠比不足月的胎兒更能接受麻醉和手術的挑戰。而且在子宮內手術，母親同時也要冒麻醉和手術的危險。在目前只有少數情形，可以在子宮內手術矯正，如兩側泌尿系統阻塞，阻塞性水腦和先天性橫隔膜疝氣等。目前仍然以引產和產後手術矯正先天性畸型兒為主要的處理方式，子宮內手術則只能針對特殊的個案。產後手術矯正臍膨出和腹壁裂，分別都可以得到71%和85%的存活率(表4)。

引產(termination)

引產一直是處理先天畸型兒的重要方法，在妊娠9-10週對有單一基因疾病病史的孕婦作絨毛採樣，可以及時診斷胎兒異常，甚至只須進行子宮擴刮術就可以處理異常胎兒。

但是在妊娠中期經由羊水穿刺或超音波檢查所發現的致死性胎兒異常，往往就要借由催生來中止妊娠。其實催生本身的過程要比子宮擴刮術要來得安全，而各種催生藥劑如PGE2的引用，更使得催生的過程十分順利。

然而，優生保健法規定胎兒異常必須在24週之前診斷並處理，超過妊娠24週，引產就不是適當合法的處理方式了。

產後處理(Postnatal management)

新生兒篩檢(newborn screening)

目前已經有一套很好的篩檢系統來找出新生兒代謝性疾病，在1991年已有90%的新生兒接受篩檢(表18)，在台灣最常見的為蠶豆症(G6PD)，其次為先天性甲狀腺功能低下(CHT)和苯酮尿症(PKU)(表19)。

蠶豆症的發生率在女生為1/111，男生為1/34，其次為先天性甲狀腺功能低下(1/3102)，和苯酮尿症(1/51880)，半乳糖血症(Galactosemia)等則為少見(表20)。

社會福利(social support)

如果唐氏症很不幸地無法在產前發現，有76%在出生1個月就會因為獨特的長相被診斷出來。

育養一個唐氏症兒，對家庭的經濟而言是一項很大的負擔，尤其是31%的唐氏症合併有先天性心臟病，耗費更大。平均每月的醫療費在台幣3000元以上。另外還要支付特殊教育，及特別照顧等等費用，每個家庭每月平均要花2萬5千元在這個唐氏症兒生上。以台灣每人每月平均所得2萬元來計算的話，如果一對夫婦要養育這個唐氏症兒，就要花掉他們一半以上的收入。

為了減輕這種負擔，有2/3的家庭轉向私人基金會求助，有13%的家庭將他們的小孩送去接受特殊教育訓練，而有6%的唐氏症兒被迫長期放置於醫療機構，而社會福利機構卻只能對5.4%的不幸家庭伸出援手。

雖然在台灣每人每年的所得已高達美金1萬元，在亞洲而言名列第6名。然而對這些殘障的小兒，卻從未提供社會支援。因為照顧這些殘障小兒要背負這麼大的經濟和心理負擔，難怪有很多殘障的胎兒和新生兒要被他們的父母在不堪負荷的情況下遺棄，台灣果然是個“富有而貪婪”之島。

手術矯正(surgical correction)

由於外科手術技巧、麻醉方式及營養的補給均大有改進，小兒科的手術預後均十分良好。然而產前正確的診斷，可以提高產後手術治癒的成功率。例如產前診斷胎便腹膜炎(meconium peritonitis)和腹壁缺損可以增進手術的成功率。

正如謝豐舟等人的報告，產前診斷和產後矯正手術一貫作業可以給先天畸型兒(如腹部及泌尿系統異常)的矯正獲得更好的手術成功率。

第一對連體嬰在1979年9月10日在台大醫院成功地分割，隨後共有9對相連程度不一的胎兒在台大進行分割。然而，對婦產科醫師而言，連體嬰的誕生實在是產前診斷最大的恥辱。

另一個台灣婦產科醫師必須要面對的問題是頭顏面的先天畸型，發生率約為2 /1000。兔唇顎裂的發生率約為1/500到1/600，這種畸型會造成餵食、語言和美觀上的問題。而外觀的問題往往會影響小孩心理的發育，因此頭顏面畸型在產後的處理，是一個很重要的課題。

因為這種畸型並不會影響生存，因此這類胎兒不應被引產，應該在胎兒出生後矯正，不過大部分的父母一旦發現懷有這種胎兒，不論週數是否大於24週，往往就將胎兒孩引產。

所幸的是長庚醫院頭顏面矯正中心的主任羅慧夫醫師(Dr. Nordhoff)，早已設立基金會來幫助這些病童，值得注意的是，這類畸型的矯治，須要許多專家的參與，不止是外科醫師進行矯正手術，還須要社工人員、語言治療家和心理學家來共同治療，而整個治療的費用可以說相當高，光手術本身可能就要台幣10萬以上。

除了唐氏症和頭顏面畸型兒有基金會外，先天性心臟病和乙型地中海貧血的病童也都有基金會來提供醫療上的援助。

雖然台灣表面上看起來很富有，社會福利仍然不盡理想。事實上真正關心這些些問題的人應該花一些錢和時間來協助這些殘障兒童過一個正常的生活。

結論(Summary)

我們相信，每個誕生的小孩應該擁有“生而正常”的權利，雖然“正常”並不容易明確地被定義出來，但是我們可以定義“正常”為“不具有重大的缺陷，”要達到這個目標，須要社會中的每一成員共同奮鬥。

大眾必須對先天畸型及它的後遺症有詳盡的了解。而在孕前做篩檢，在懷孕中做完整的產前遺傳診斷，是每個孕婦應該要得到的照顧。在產前診斷、新生兒照顧和新生兒手術等各方面，現在都有長足的進步，不過由於醫療資源的不平均分布，將來在台灣中部、南部、東部各籌設一個產前診斷的中心可以說是當務之急。

誌謝：

謹向衛生署保健處，榮民總醫院楊勉力主任，成功大學林秀娟醫師，高雄醫學院趙美琴醫師提供本文珍貴料誌謝。

表1 台灣地區新生兒死因

Table 1. Causes of neonatal death in Taiwan

	第一 1st	第二 2nd	第三 3rd
1960	早產 prematurity(50%)	感染 infection(22%)	寄生虫 parasite(14%)
1970	感染 infection(30%)	早產 prematurity(28%)	肺部發育不全 RDS(11%)
1980	週產期原因 perinatal(50%)	先天畸型 malformation(16%)	肺炎 penumonia(15%)
1990	週產期原因 perinatal(54%)	先天畸型 malformation(31%)	敗血症 sepsis(4%)

資料來源：衛生署，衛生統計，1991年
Source: Health statistics, Department of Health, 1991
RDS: respiratory distress syndrome

表2 台灣地區嬰兒死因

Table 2. Causes of infant death in Taiwan

	第一 1st	第二 2nd	第三 3rd
1960	早產 prematurity(25%)	腸胃道感染 GI infection20%	肺炎 pneumonia19%
1970	早產 prematurity(16%)	氣管炎 bronchitis 15%	其他感染 other infections14%
1980	肺炎 pneumonia(23%)	週產期原因 perinatal cause21%	先天畸型 malformation19%
1990	先天畸型 malformation(30%)	週產期原因 perinatal cause24%	意外 accident12%

資料來源：衛生署，衛生統計，1991年
Source: Health statistics, Department of Health, 1991

表3 台灣地區先天畸型的發生率

Table 3. Incidence of congenital malformation in Taiwan

	百分比 percentage
1955-1962	0.87
1965-1968	1.32
1971-1975	0.82
1977-1978	0.67
1986-1990	1.40

資料來源：衛生署，衛生統計，1991年
Source: Health statistics, Department of Health, 1991

表4 產後手術矯正腹壁裂的預後

Table 4. Outcome of the postnatal correction of abdominal wall defects

	臍膨出 Omphalocele	腹壁裂 Gastroschisis
數目 Number	31	54
存活率 Survival rate	71%	85%
畸型率 Malformation rate	54%	6%
矯正率 Primary fascial closure	85%	87%

資料來源：
Source: Chang PY: Experience with treatment of gastroschisis and omphalocele. J Formosan Med Assoc 1992;91:447-51.

表5 中樞神經系統畸型率 (每1000個活產兒)

Table 5. Incidence of anomalies of the central nervous system (per 1000 births)

	台大 NTUH	衛生署 81-85	衛生署 86-89	高醫 KMC	長庚 CGMH
無腦 Anencephaly	1.29	0.40	0.40	0.78	1.02
水腦 Hydrocephaly	0.51	0.19	0.28	0.19	0.35
空腦 Holoprosencephaly	0.16				0.02
腦膨出 Encephalocele	0.15	0.10	0.14		0.14
脊柱裂 Open spina bifida	0.13	0.10	0.14		0.07
小腦 Microcephaly	0.09			0.58	
腦膜膨出 Meningocele					0.11
其他 Others					0.11

NTUH: National Taiwan University Hospital, KMC: Kaohsiung Medical College, CGMH: Chang Gung Memorial Hospital

表6 頭顏面畸型率(每1000個活產兒)

Table 6. Incidence of craniofacial defects

	台大 NTUH	衛生署 81-85	衛生署 86-89	高醫 KMC	長庚 CGMH
兔唇+顎裂 Cleft lip+palate	1.49	0.85	0.77	0.97	1.02
兔唇 Cleft lip		0.22	0.30	0.58	0.36
顎裂 Cleft patate		0.60	0.32	0.58	0.36
眼距過寬 Hypertelorism					0.05
其他 Others					0.14

NTUH: National Taiwan University Hospital, KMC: Kaohsiung Medical College, CGMH: Chang Gung Memorial Hospital

表7 腸胃系統畸型率（每1000個活產兒）

Table 7. Incidence of anomalies of the gastrointestinal system

	台大 NTUH	衛生署 81-85	衛生署 86-89	高醫 KMC	長庚 CGMH
氣管食道廔管 Tracheoesophageal fistula					0.09
無肛症 Imperforate anus	0.33	0.22	0.28	0.19	0.30
腸阻塞 Intestinal obstruction	0.24			0.19	0.16
其他 Others					0.14

NTUH: National Taiwan University Hospital, KMC: Kaohsiung Medical College, CGMH: Chang Gung Memorial Hospital

表8 肌肉骨骼系統異常率（每1000個活產兒）

Table 8. Incidence of anomalies of the musculo-skeletal system

	台大 NTUH	衛生署 81-85	衛生署 86-89	高醫 KMC	長庚 CGMH
末端異常 Distal anomalies	0.67	0.36	0.74	3.89	1.50
內翻／外翻 Inversion/eversionleg	0.15				0.27
侏儒 Dwarfism	0.16				0.09
成骨不全 Osteogenesis imperfecta	0.07				0.02
四肢發育不良 Limb dysplasia					0.25

NTUH: National Taiwan University Hospital, KMC: Kaohsiung Medical College, CGMH: Chang Gung Memorial Hospital

表9 泌尿系統畸型率（每1000個活產兒）

Table 9. Incidence of anomalies of the genito-urinary system

	台大 NTUH	衛生署 81-85	衛生署 86-89	高醫 KMC	長庚 CGMH
尿道下裂 Hypospadia	0.27	0.43	0.4	0.36	0.18
外生殖器不明 Ambiguous genitalia	0.15				
水腎 Hydronephrosis	0.13				0.30
囊狀腎 Cystic Kidney	0.09			0.19	0.18
腎發育不全 Dysplastic Kidney	0.05			0.19	0.07
美克氏症候群 Meckel's syndrome	0.02				

NTUH: National Taiwan University Hospital, KMC: Kaohsiung Medical College, CGMH: Chang Gung Memorial Hospital

表10 腹壁缺損率（每1000個活產兒）

Table 10. Incidence of abdominal wall defects

	臺大 NTUH	長庚 CGMH
腹壁裂 Gastroschisis	0.09	0.32
臍膨出 Omphalocele	0.09	0.23
橫膈疝氣 Diaphragmatic hernia		0.20

NTUH: National Taiwan University Hospital, CGMH: Chang Gung Memorial Hospital

表11　高齡產婦接受羊水穿刺檢查率

Table 11. Genetic amniocentesis for advanced maternal age

	34歲以上產婦 >34Y delivery	接受羊水穿刺個案數 cases of amniocentesis	百分比 %
1987	8752	672	7.7
1988	10577	1163	11.0
1989	11695	1828	15.6
1990	12927	2214	17.1

Source: Health statistics, Department of Health, 1991
Y: year-old

表12　羊水穿刺檢查胎兒異常率

Table 12. Results of genetic amniocentesis

	總數 Total no.	不正常個案數 abnormal no.	百分比 %
1986	2237	64	2.9%
1987	1197	46	3.8%
1988	2336	72	3.1%
1989	2975	106	3.6%
1990	3558	95	2.7%
1991	3070	123	4.0%

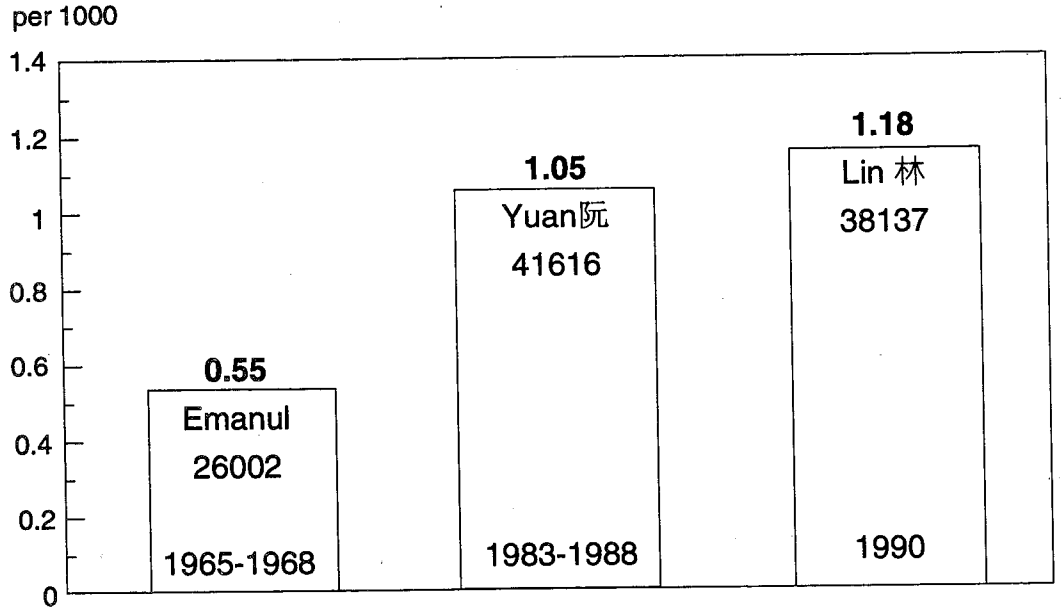
Source: Health statistics, Department of Health, 1991

表13　羊水穿刺檢查之染色體異常率
Table 13. chromosomal aberration in amniocentesis

	長庚 CGMH	台大 NTUH	榮總 VGH	總合 total
接受羊水個案 Amniocentesis	2488	2975	4062	9525
染色體異常率 Abnormal rate	2.37%	2.99%	2.50%	2.62%
數目異常 Numeric	58.0%	59.6%	54.5%	57.4%
唐氏症 (Trisomy 21)	(16%)	(27%)	(22%)	(22%)
構造異常 Structural	42.0%	40.4%	45.5%	42.6%

CGMH: Chang Gung Memorial Hospital, NTUH: National Taiwan University Hospital, VGH: Veterans General Hospital

表14　台灣地區唐氏症之發生率
Table 14. Incidence of Down syndrome in Taiwan



Source: Emanul:Incidence of malformations in Chinese population. Teratology 1971;5:159-70. Yuan(阮正雄)：Down syndrome. Manucipal report of Taipei 1988. Lin (林秀娟)：Survey of Down (unpublished data)

表15 臍血採樣術的適應症
Table 15. Indications for percutaneous ultrasound guided fetal blood sampling

非免疫性胎兒水腫 Nonimmune hydrops fetalis	36%
胎兒疑似血友病 Suspected fetal hemophilia	3%
胎兒疑似德國麻疹感染 Suspected fetal rubella infection	23%
胎兒疑似地中海型貧血 Suspected fetal beta-thalassemia major	2%
胎兒疑似構造異常 Suspected fetal structural abnormalities	34%
重度子宮內生長遲滯 Severe intrauterine growth retardation	1%
羊水染色體結果不正常 Suspicious amniotic fluid karyotype	1%

資料來源：
Source: Hsieh F J: Percutaneous ultrasound-guided fetal blood sampling: Experience in the first 100 cases. J Formosan Med Assoc 1989;88:137-42.

表16 產前診斷先天性心臟血管系統畸型
Table 16. Prenatally diagnosed cases of congenital cardiovascular malformation

心內墊缺損 ■Endocardiac cushing defect:	8
法洛氏症候群 ■Tetralogy of Fallot:	4
心臟血管發育不全 ■Hypoplastic heart syndrome:	4
Ebstein's氏畸型 ■Ebstein's anomaly:	3
心臟腫瘤 ■Cardiac tumor:	2
肺動脈狹窄 ■Pulmonary stenosis:	2
心房心室中隔缺損 ■Atrial and ventricular septal defects:	2
大血管轉位 ■Transposition of great arteries:	1
三尖瓣缺損 ■Tricuspid atresia:	1
微小心室中隔缺損 ■Tiny, small ventricular septal defect:	20
連體嬰 (心臟相連) ■Cardiac-cardiac connection (conjoin twin)	2

表17 產前診斷心律不整

Table 17. Prenatally diagnosed cases of arrhythmia

心房過早收縮 ■Atrial premature contraction:	43
心室過早收縮 ■Ventricular premature contraction:	9
心房顫動合併房室阻斷 ■Atrial fibrillation with block:	2
2比1房室阻斷 ■2:1 Atrio-Ventricular block:	4
3比1房室阻斷 ■3:1 Atrio-Ventricular block:	2
完全房室阻斷 ■Complete block:	1
竇性心律不整 ■Sinus arrhythmia:	1

表18 台灣地區新生兒篩檢

Table 18. Neonatal screening for metabolic disease in Taiwan

	生產數 birth no.	接受篩檢數 screen no.	百分比 %
1984	396725	23647	6.7%
1985	345053	38538	11.2%
1986	308187	73666	23.9%
1987	313062	124257	39.7%
1988	341054	191956	56.3%
1989	314553	214477	68.2%
1990	334871	266312	79.5%
1991	321271	282934	88.0%

Source: Health statistics, Department of Health, 1991

表19　新生兒篩檢發現之代謝異常

Table 19. Cases of inborn errors of metabolism found by neonatal screening

	苯酮尿症 PKU	先天性甲狀腺功能低下 CHT	蠶豆症 G6PD	半乳糖血症 Galactosemia	高胱氨酸尿症 Homocystinuria
1984	13	-	0	0	
1985	3	9	-	1	0
1986	0	24	-	0	1
1987	2	43	244	3	2
1988	2	72	1665	1	-
1989	5	79	2605	7	0
1990	5	71	3379	0	2
1991	9	105	44.0	1	2
total	27	4.6	12323	13	7

資料來源：衛生署，衛生統計，1991
source: Health statistics, Department of Health, 1991

表20　台灣地區新生兒代謝異常之發生率

Table 20. Prevalence of inborn errors of metabolism in Taiwan

苯酮尿症 Phenylketonuria	1/51800
半乳糖血症 Galactosemia	1/186770
先天性甲狀腺機能低下 Congenital HT	1/3102
高胱氨酸尿症 Homocystinuria	1/77821
蠶豆症 G6PD	F:1/111, M:1/34

資料來源：衛生署，衛生統計，1991
source: Health statistics, Department of Health, 1991
HT: hypothyroidism, G6PD: glucose-6-phosphatase deficiency, F: female, M:male

圖1　台灣地區年出生數

Figure 1.　Annual births in Taiwan

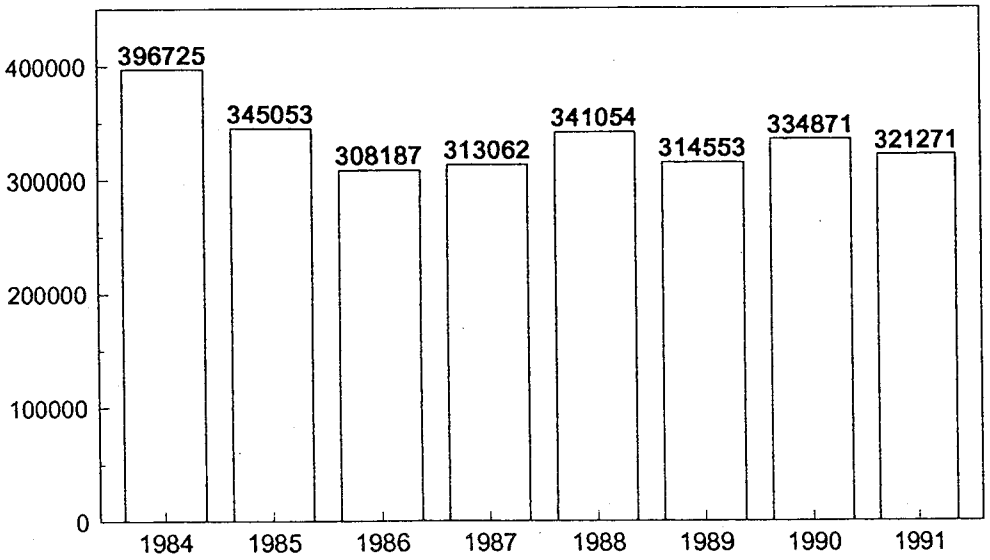


圖2　台灣地區先天畸型發生率

Figure 2.　Congenital malformation surveillence in Taiwan

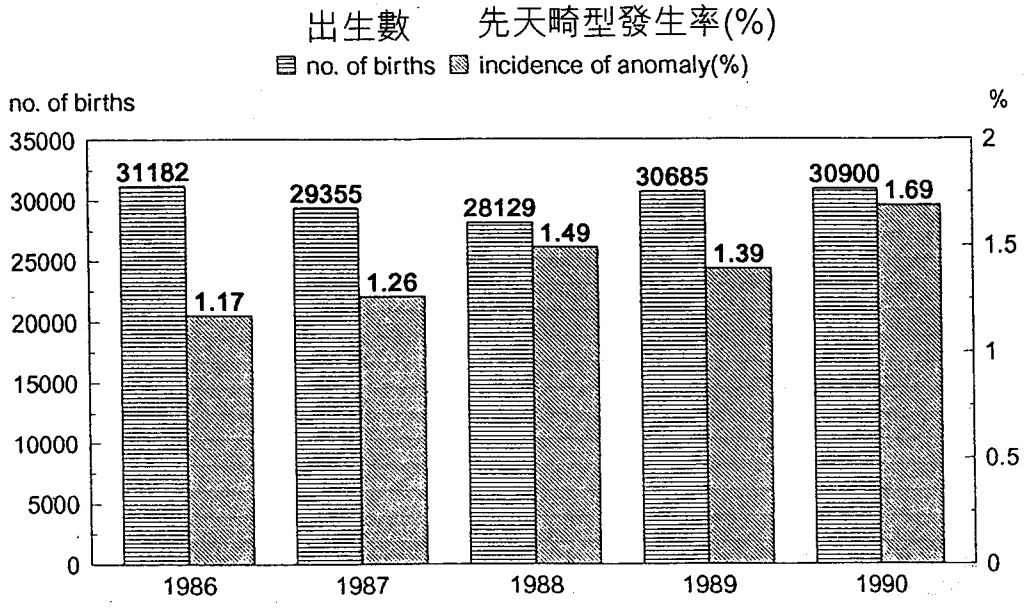


圖3　各年齡層婦女產下唐氏症兒的比例

Figure 3. Percentage of women in the population delivering a Down or normal baby

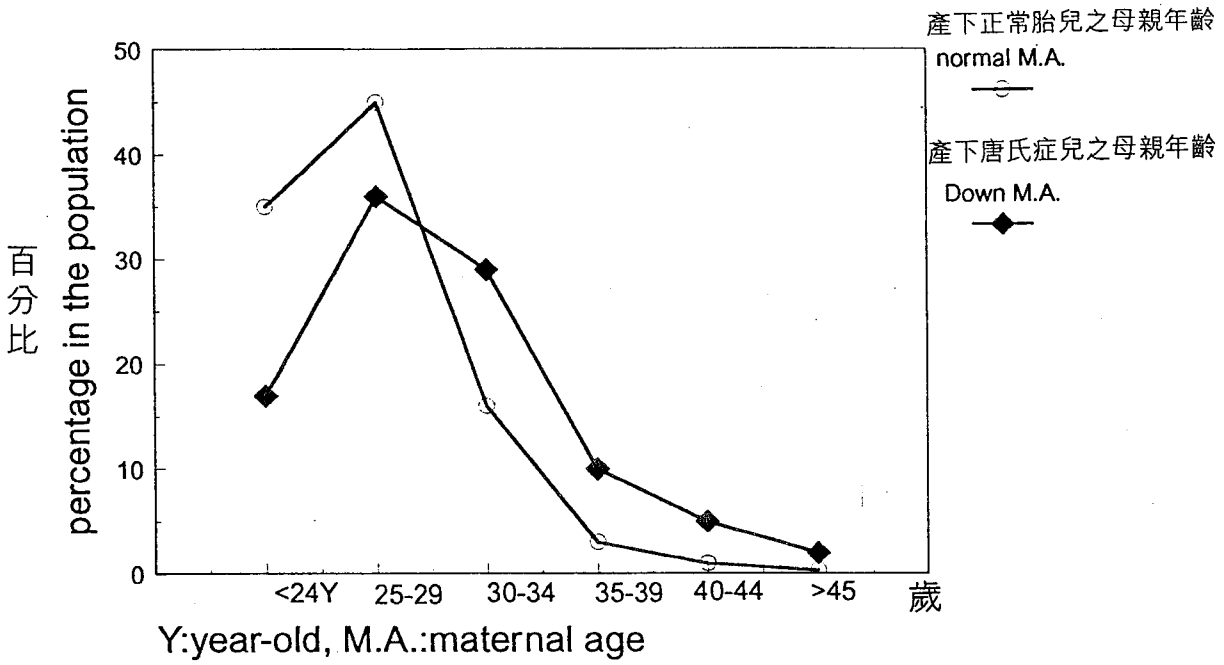


圖4　地中海型貧血篩檢系統

Figure 4. Thalassemia screening system

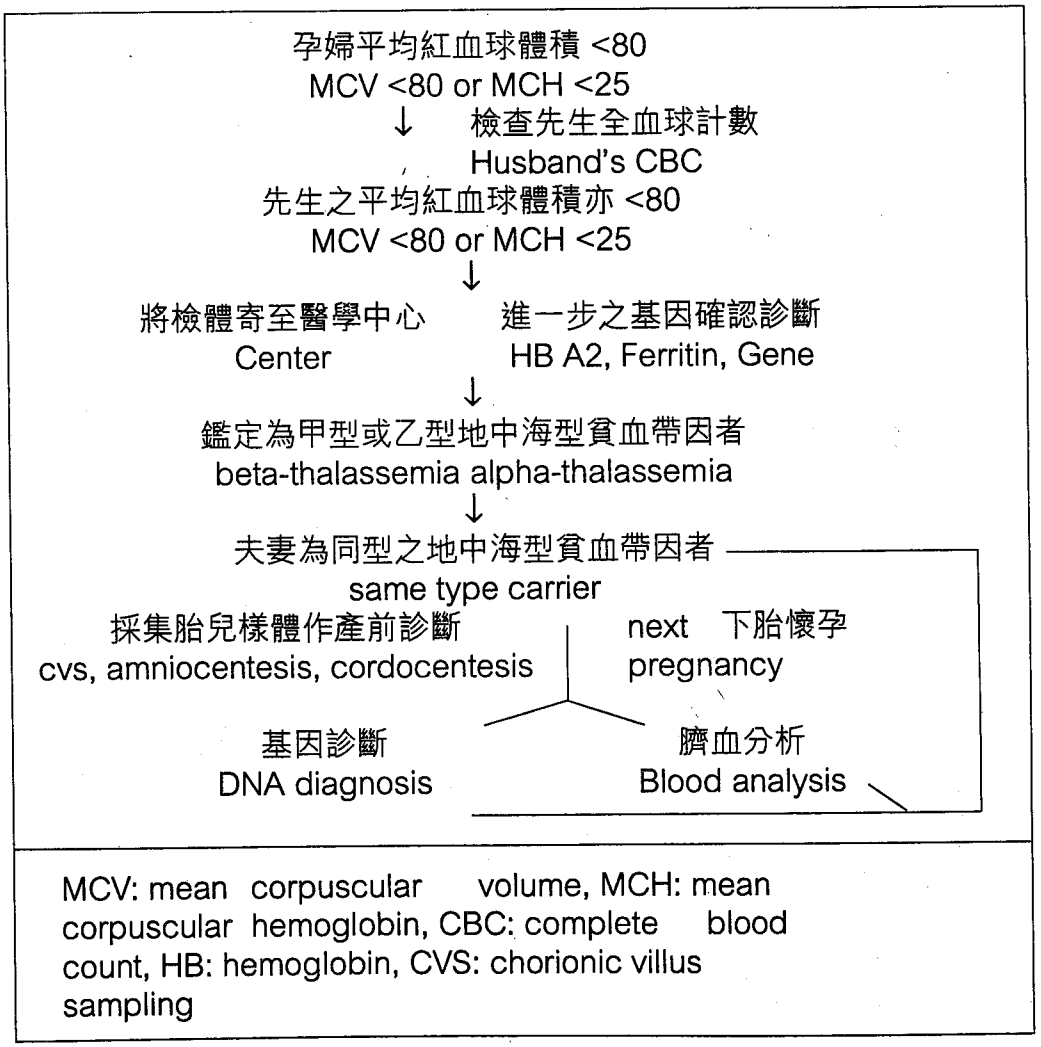


圖5　中華民國超音波學會會員分布圖

Figure 5.　Members of the society of Ultrasound in Medicine, Republic of China