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# Congenital Malformations in Singapore

by

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## Introduction

The criteria for a so-called "normal" human being embrace a wide range of characteristics over which there is no common agreement among different workers. The epithelial "pearls" in the palate of the newborn are seen in about 20% in Kandang Kerbau Hospital while miliaria are seen in only 2-5%. Would the former be normal and the later abnormal? What about mongolian spots, mild cases of talipes and bat-ears, small phalluses in male infants, scanty or exuberant scalp hair, etc. The other problem about identification of malformations is that many deformities are difficult or almost impossible to detect at birth, *e.g.* some forms of congenital heart disease, hypothyroidism, adrenal hyperplasia in the newborn male, glucose-6-phosphate deficency in the erythrocyte, *etc.* so that figures of incidence of various types of congenital malformations may vary widely in different areas not necessarily due to the intrinsic differences in incidences but due to the factors above and other factors, such as the preferred personal interest of the doctor with regard to some particular congenital malformation. Therefore published figures should always be looked at taking into consideration all the above factors.

## Mechanisms in Congenital Defects

The normal foetus is formed by a process of growth and resorption at correct sites and at the correct times and any deviation from these very critical arrangement may result in congenital deformities. Certain mechanisms are commonly deranged and they include:

### 1. Too little growth

The lips and palate are formed formed from the fusion of two halves and failure of growth with fusion will result in cleft lip and cleft palate. Similary, failure of fusion of the anterior abdominal wall will result in various degrees of exomphalos and ectopic vesicae.

### 2. Too little resorption

Several structures are formed by excessive growth followed by resorption of excessive tissue to "cut it down" to the correct size. This is seen pre-eminently in the gut which at one stage is a solid cylinder and later there is canalisation. Failure of such canalisation will result in stenoses or atresias of the intestinal canal *e.g.* oesophageal atresia, duodenal or jejunal atresias.

### 3. Too much resorption

Sometimes this resorptive process is too much and goes on in an unrestrained manner. An example is the resorption of the septum primum to form an efficient valve for the foramen ovale together with the septum seccundum. If the resorptive process is excessive, then we get an incompetent valve of the foramen ovale.

### 4. Resorption in the wrong location

Sometimes there should be no resorption in a particular structure which, however, undergoes resorption wrongly. The cribiform openings in the septum primum in cases of atrial septal defect is an example of this.

### 5. Growth of normal character but in an abnormal position.

Sometimes again the normal growth process is correct but at the wrong spot, *e.g.* the truncus septum which divides the truncus arteriousus with the aorta and the pulmonary artery into almost 2 equal channels, however, it may be misplaced giving rise to a small pulmonary artery and an enarged aorta.

## Aetiology

It is when one comes to consider the causes which operate to produce these aberrant mechanisms of growth and resorption that difficulties arise. Obviously, there must be a cause for a malformation as it is abnormal, yet in many instances, it is impossible to find the cause. Research into the causes is not just academic because prevention may be possible once the cause is known.

### 1. Early Theories

Many of the earlier theories in the causation of congenital defects are without scientific basis. Supernatural influences were very popular and in fact still are in this country—a punishment from the gods. In ancient times, the poor infant and the mother were sometimes sacrificed as a result. Intercourse during menstruation was another popular theory. Visual experiences of the mother during pregnancy such as seeing of "spirits", ugly animals, frightening sights, *etc.* are transmitted to the image of the foetus who is then supposed to assume the form of the freak.

### 2. Present Ideas

A lot of the modern ideas have stemmed from animal experimentation but the projection of the findings to human beings is not necessarily correct. The ability to culture human choromosomes has done much to elucidate genetic cuses. A summary of the possible causes of congenital malformations is given in Fig. 1.

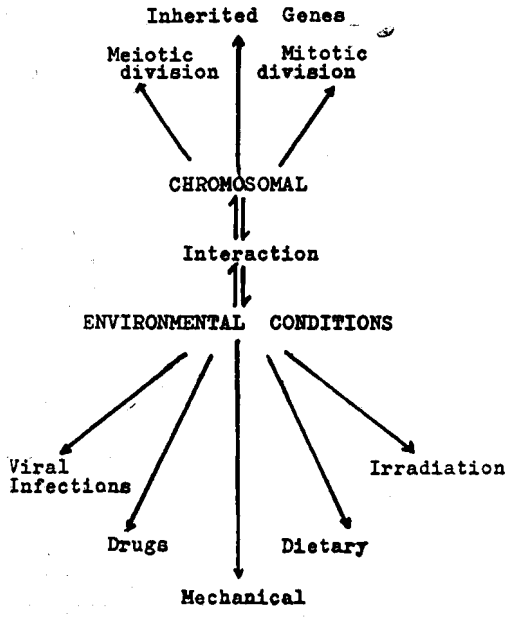
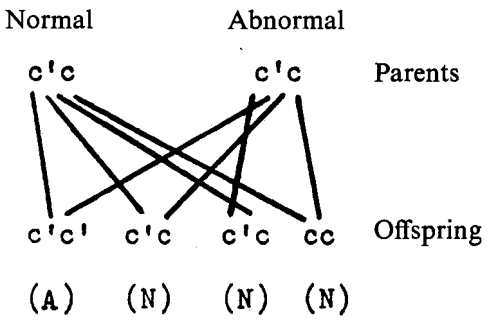



**Fig 1**

### 1. Chromosomal causes

From family studies it was discovered a long time ago that some congenital malformations are definitely inherited. Since each chromosome has its pair, each gene responsible for a particular character has its pair and residing in identical loci in the pair of chromosomes. Normally, both genes are normal and the person shows the normal character. If one of the genes is abnormal then the character can be abnormal or it can be normal. When the character is abnormal, the gene is said to be *dominant*. However, if the character is normal with possession of one abnormal gene but abnormal with the of one abnormal gene but abnormal with the possession of 2 abnormal genes, then the gene is said to be *recessive*. The implications of inheritance with dominant and recessive genes can be simply illustrated thus. Let $c$ represent a gene determining a normal character, and $c'$ represent an abnormal gene. In *dominant inheritance*, suppose one of the parents has the genetic constitution $c'c$ and the other normal $cc$. The offsprings are illustrated in Fig. 2:-




(N)=Normal

(A)=Abnormal

**Fig. 2**

Therefore ½ the offspring will be abnormal and ½ will be normal. Similarly, in *recessive inheritance* (Fig. 3):

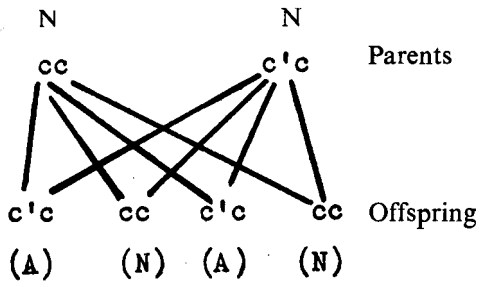



**Fig. 3**

Therefore $\frac{1}{4}$ will be normal and $\frac{3}{4}$ "normal". However, of the "normals" 2/3rds are carriers as are the parents. Carriers are persons who have a recessive abnormal gene but do not show the abnormality but have a propensity to pass on the abnormal gene to their offspring.

Some of the congenital malformations inherited in a dominant fashion include microspherocytosis, polydactyly, *etc.* and those inherited in a recessive manner include alcaptonuria, congenital ichthyosis, spira bifida, *etc.* The above deformities result in an offspring where the abnormal gene or chromosome is already present in one or both parents.

There a group of malformations due to abnormal chromosomal structure or number but where the parental chromosomes are normal. The abnormality in the chromosomes arise during the chromosomal division in the formation of the gametes, *i.e.* the sperms or the ova, a process called *meiosis.* The abnormality can also arise after fertilisation *i.e.* after formation of the zygote *i.e.* during *mitosis.* One of the ways whereby abnormalities in chromosome number can occur in meiosis or mitosis is termed *non-disjunction.* Taking the sex chromosomes as an example (XY=male and XX=female) at meiosis normal disjunction would produce X or Y-bearing sperms but all the ova will be X-bearing (Fig. 4):


**Fig. 4**

However, in non-disjunction, instead on one chromosome going to each of 2 gametes, sometimes for some reason or other, both chromosomes go to one gamete and the other has none

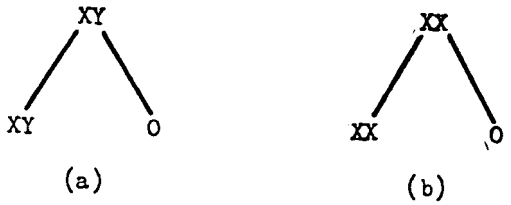



**Fig. 5**

(Fig. 5): (a) Non-disjunction in male; (b) Non-disjunction in female. If such an abnormal female gamete fertilises a normal male gamete, the possible results are as shown in Fig. 6 There

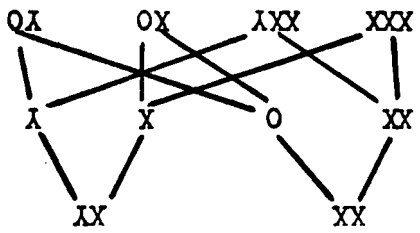



**Fig. 6**

may be a triple-X female (XXX), a Klinefelter (XXY), a Turner's (XO) while YO is supposed to be lethal. Similarly, such abnormalities may arise when an abnormal male gamete mates with a normal female gamete.

In the same manner, non-disjunction may occur very early on in mitosis after the formation of the zygote with production of chromosomal congenital defects.

Not only may the sex chromosomes be abnormal in this fashion but also the non-sex chromosomes, or autosomes, again with resultant production of congenital malformations. The classical Mongol or trisomy 21, *i.e.* an individual with 47 chromosomes, the extra one being chromosome 21, arises because of non-disjunction during meiosis at gametogenesis or during mitosis after formation of the zygote. However, there is another type of Mongol, the translocation Mongol where the abnormal chromosome is transmitted from the parents themselves, this being an example of direct inheritance. Two

other types of autosomal chromosome defects have also been encountered here, namely trisomy 16-18, and trisomy 13-15. In both these conditions, there are 47 chromosomes, the extra chromosome being in the group 16-18 or 13-15 respectively. In the 16-18 trisomy, the clinical features are definite enough for the condition to be suspected even clinically and they include low-set ears, micrognathus, prominent occiput, peculiar posture of the fingers, rocker-bottom feet and other associated abnormalities (Fig. 7):

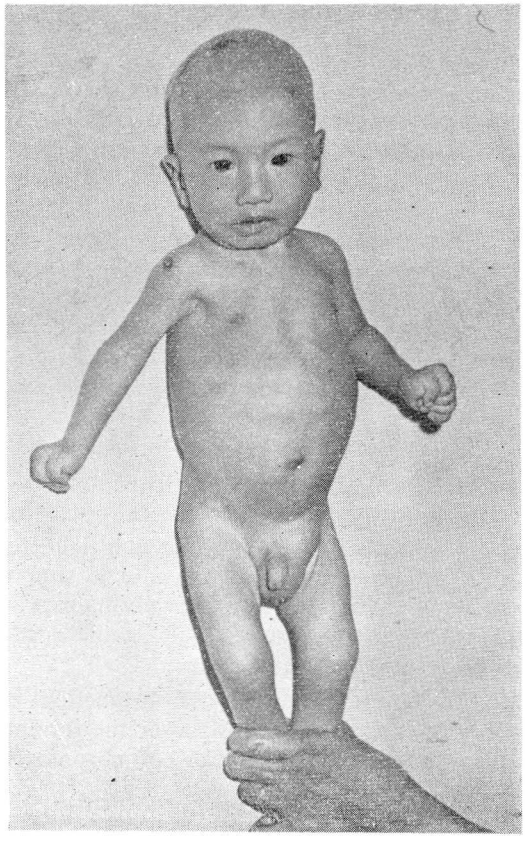


**Fig 7. 16-18 Trisomy. Note the micrognathus, low-set-ears, peculiar posture of fugures.**

**Fig. 7**

The 13-15 trisomy syndrome superficially resembles the 17-18 trisomy but has in addition cleft lip and palate, microphthalmia (Fig. 8): In both these trisomies 13-15 and 16-18, the fault is in meiosis or mitosis and not intrinsically due to transmitted abnormal chromosomes from the parents themselves.

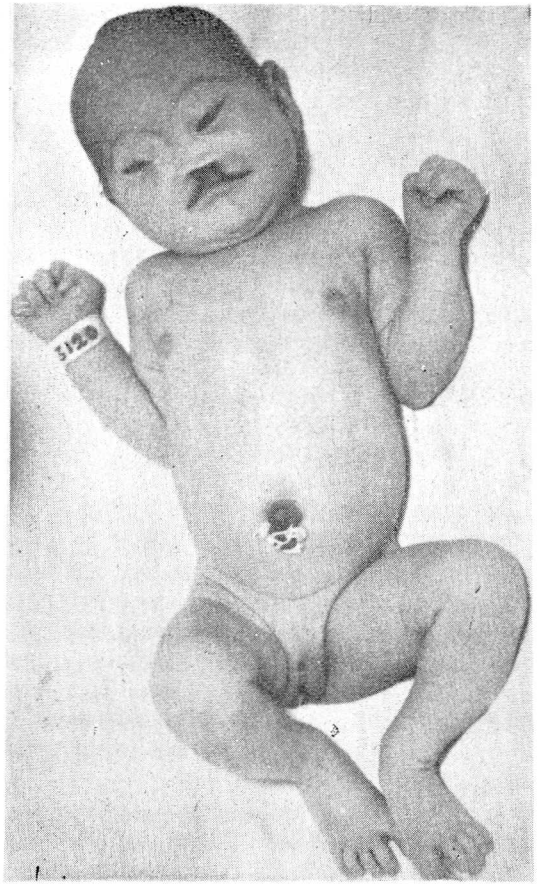


**Fig 8. 13-15 Trisomy. Note the cleft lip and palate and attitude of fingers.**

**Fig. 8**

Summarising then, congenital malformations due to chromosomal defects may be transmitted by the parents themselves who possess these abnormal chromosomes, or the chromosomal defects may arise during gametogenesis or after the formation of the zygote, the latter aberration probably being due to environmental factors.

## 2. Environmental conditions

For environmental conditions to result in the formation of a congenital deformity, the factor or factors must act during the first trimester of pregnancy when organogenesis is taking place. As most of these defects are reported to be due to certain environmental causes on circumstantial and statistical evidence rather than direct proof

it is difficult to be categorical about them. However, the following are some of the factors which have been incriminated:

*a*) **Viral Infections:**

1. *Rubella:* Since the observations of Gregg and Swan, there seems no doubt that German Measles in the first trimester may give rise to congenital defects such as cataracts, congenital heart disease, deafness and microcephaly. However, the incidence of such defects is not very certain; approximately 20% may develop these defects. One of the difficulties, is the certain diagnosis of rubella, which clinically may mimic other conditions, especially allergy in association with a rash.
2. *Measles:* Classical measles is rare in the child-bearing age and therefore there is an insufficient number of cases to decide whether it is tertogenic or not.
3. *Influenza:* Several prospective studies have been done regarding infection during the first trimester and in influenza epidemics. So far, the figures are not statistically significant.
4. *Infective hepatitis:* There is no statistical evidence complicating the virus as a cause of congenital malformations.
5. *Chicken pox:* Similarly, there is no evidence that the virus causes deformities.
6. *Vaccinia:* So far, there is no statistical proof that vaccination against smallpox during the first trimester is a cause of congenital malformations.
7. *Mumps:* There is no proof that mumps contracted during the first trimester would induce malformations in the foetus.

Summarising, then rubella is probably the only virus disease which is known to produce congenital malformations in the foetus if the mother contracts the disease early on in pregnancy.

*b.* **Irradiation:**

Irradiation of the rat foetus has produced cleft palate and skull defects, and work on therapeutic irradiation of the pelvis for malignancy before conception and after conception have produced statistically significant greater numbers of malformations after conception has occured. The epidemiological studies of pregnant mothers exposed to the atom bombs in Hiroshima and Nagasaki have provided evidence that gamma rays can produce congenital malformations. In humans, the most consistent defect is microcephaly, and this is consistent with the observation in animals that the primitive nerve cells are more sensitive to radiotherapy than fully developed neurones.

*c.* **Dietary deficiency:**

A large amount of work in this direction has been carried out on pregnant animals fed on diets known to be deficient in certain food constituents. However, the specificity of action of the deficient constituent in the production of specific defects does not necessarily hold for different animals. For example, hypovitaminosis causes anophthalmia and microphthalmia in the sow, but produces hydrocephalus in the rabbit. Ariboflavinosis in the rat produces skeletal defects and cleft palate while in the mouse it produces skeletal defects, oesophageal dysplasia, cerebral defects and hydrocephalus.

However, dietary deficiency as a cause of foetal malformations, is difficult to prove. The statistical study of infants of "poor" and "well-to-do" mothers in a maternity unit may be enfeebled by the fact that extraneous factors may also play a part.

*d.* **Mechanical:**

Mechanical pressure in utero as a cause of some congenital deformities is possible in talipes. It has been proposed by Denis Browne (1951) that many cases of talipes are due to abnormal intra-uterine posture of the foetal legs and we paediatricians are familar with the manner in which newborn infants can be refolded into prenatal postures. Another common defect which may be due to mechanical factors is genu recurvatum.

Facial asymmetry may be due to mechanical pressure.

*e.* **Drugs:**

The role of drugs in the production of malformations did not receive much attention till only recent times with the advent of thalidomide and its tragedy. Prior to thalidomide, a few drugs had been known to be causative agents.

1. *Antifolic agents:* These agents when used in the chemotherapy of malignant disease have been known to produce malformations and this was thought to be due to its antifolic acid activity so that in effect it was a dietary deficiency. Aminopterin and methotrexate are 2 common antifolic agents.
2. *Oral progestins:* The use of 17-ethinyl testosterone and 17-ethinyl-19-nor-testosterone in the prevention of abortion has produced masculinisation in female infants, *i.e.* one form of female pseudohermaphrodite.
3. *Antithyroid compounds:* Rarely, the antithyroid drugs used in the thyrotoxic pregnant mother have resulted in infants with goitre and hypothyroidism.
4. *Stilboesterol:* Oddly enough, large doses of stilboesterol have produced masculinisation of female foetuses. It has been suggested that this stimulated the production of increased androgens from the foetal adrenals or the mothers concerned may be abnormal "metabolizers" of oestrogen with the production of substances with masculinising activity.
5. *Adrenal corticosteroids:* Many mothers who suffer from diseases which would usually end in death or failure of pregnancy, now are able to conceive and bear children. In these diseases, the corticosteroids are given in large pharmacological doses, and it is surprising that very few congenital malformations have resulted from its use. Occasionally, infants with cleft palate may be born.
6. *Thalidomide:* Thalidomide is a sedative produced in Germany and released in 1958 and was used widely in Continental Europe and then was taken up in England and was popularly prescribed also to preganant women. The malformation produced involved mainly the limbs—so-called phocomelias. However, associated defects included malformations of the external ear, microphthalmias, duodenal stenosis, anal atresias and congenital heart disease. It is estimated that in the Federal Republic of Germany itself, there are 5,000 cases of thalidomide-produced malformations. The most sensitive period is between the 27th and 44th day after conception. (Weicker, 1962)

Since thalidomide, many drugs taken in early pregnancy have coincided with the delivery of a malformed child but so far, these have been limited to single case reports and they have not been proved to be definitely causative factors. Anyway, thalidomide has taught a lesson to all doctors to be very circumspect when prescribing drugs for pregnant women in the first trimester.

## Congenital Malformation in Singapore

There have been no previous study of congenital malformations in Singapore, and therefore an attempt was made to find out the types of congenital malformations met with here and the relative incidence if possible. The study covered 3 years, 1961 to 1963, and involved a total of *128,223 deliveries* comprising 34,571 Chinese, 3,591 Indians and 5,901 Malays in Kandang Kerbau Hospital. Only obvious congenital malformations will be considered, *i.e.* obvious enough for the attending obstetrician, nurses and midwives to spot and refer to the paediatrician. Many congenital malformations which manifest themselves later in infancy like some forms of congenital heart disease are excluded and nearly all the malformations are of such a nature that life in some way or other is affected. Malformations which are so minor that they are considered normal such as mongolian spots, small crooked finger, *etc.* are excluded. But abnormalities such as deformed external ears, polydactyly, *etc.* though relatively minor have been included. In this survey, the figures obtained will definitely be slightly on the low side due to underestimation. However, there is no relative bias between one type of malformation and

another since no particular congenital deformity was concentrated on during this period.

1. **Overall incidence:**

In this survey, the incidence of congenital malformations is 1.3%. In comparison, a survey conducted in the Royal Women's Hospital in Melbourne (Pitt, 1962) over a period also of 3 years covering *22,364 births* is 1.51%. Even allowing for the possibility of underestimation, the figure in Singapore does not seem to be higher than in Australia.

2. **Incidence of certain malformations:**

Certain malformations have been selected and their incidence compared with that of other countries to see if there is any racial differences. Table I illustrates this, the figures referring to number of cases per thousand births.

TABLE I

| Author | Place | Spina bifida | Hydro-cephalus | Anence-phaly | Cleft lip | Mongo-lism |
|---|---|---|---|---|---|---|
| McIntosh (1954) | New York | 1.57 | 0.87 | 1.40 | 0.87 | 1.92 |
| Caffey & Jessop (1959) | Dublin | 4.20 | 3.50 | 5.10 | 0.88 | 0.64 |
| Pleydell (1957) | Northamp-tonshire | 1.86 | 0.45 | 0.87 | 1.57 | 1.63 |
| Ivy (1957) | Pennsylvania | 0.59 | 0.16 | 0.16 | 1.06 | 0.22 |
| Edwards (1958) | Scotland | 1.70 | 1.90 | 2.80 | — | — |
| Pitt (1961) | Melbourne | 1.08 | 0.54 | 0.58 | 1.25 | 0.98 |
| Neel (1958) | Japan | 0.20 | 0.19 | 0.63 | 2.68 | — |
| Wong (1964) | Singapore | 0.17 | 0.12 | 0.21 | 1.36 | 0.88 |

*a.* **Spina bifida, hydrocephalus and anencephaly:**

Regarding these 3 CNS defects, the incidence in Japan and here seems to be much lower than in U.K. and America. Error in diagnosis here in all centres is highly unlikely as these defects are obvious and can hardly be missed. The incidence of spina bifida in some areas in England is as high as 5 per thousand (Lawrence & David, 1963).

*b.* **Cleft lip:**

This includes cleft lip alone or in association with cleft palate and again there is hardly any opportunity for error in diagnosis and the condition is obvious. The incidence here is the same as in the West which is generally quoted as 1 in 500 to 1 in 1,000 births. The distribution of the condition in Singapore is as follows: See Table 2.

From the above it is seen that it is 1.6 times commoner in males than females, but there is no racial difference taking into consideration the number of deliveries in the 3 years among the 3 races.

*c.* **Cleft palate:**

The distribution and incidence of cleft palate alone among the different races and sexes is shown in Table 3.

**TABLE 2: Cleft lip + cleft palate**

| Year | Chinese | Malays | Indians | Male | Female | Total |
|---|---|---|---|---|---|---|
| 1961 | 47 | 4 | 0 | 34 | 17 | 51 |
| 1962 | 48 | 6 | 6 | 33 | 27 | 60 |
| 1963 | 42 | 9 | 11 | 35 | 27 | 62 |
| Total: | 137 | 19 | 17 | 112 | 71 | 173 |

**TABLE 3: Cleft palate**

| Year | Chinese | Malays | Indians | Male | Female | Total |
|---|---|---|---|---|---|---|
| 1961 | 5 | 0 | 0 | 4 | 1 | 5 |
| 1962 | 18 | 0 | 0 | 8 | 10 | 18 |
| 1963 | 8 | 2 | 2 | 3 | 9 | 12 |
| Total: | 31 | 2 | 2 | 15 | 20 | 35 |

During the 3 years, there are 9 times as many Chinese infants delivered compared to Indians, and 7 times as many Chinese as Malays. The above figures show that there might be an increased incidence of cleft palate in Chinese babies when compared to Malay and Indian infants. The overall incidence works out at *0.28 per thousand* compared with a figure of *0.22 per thousand* in Melbourne (Pitt, 1962).

*d.* **Mongolism:**

Table 4 illustrates the distribution of Mongolism among the 3 races:

There is definite underestimation in this condition and it can be missed by the obstetric staff and the figure of 0.88/1,000 then would indicate the incidence of Mongolism is the same here and in the West. It is found equally in both sexes and all the 3 races.

Mongolism is one of the few congenital defects where the cause has been found, namely, a chromosomal defect, the defect being the presence of an additional chromosome—chromosome 21 and hence the condition is referred to as trisomy-21 (Fig.9).

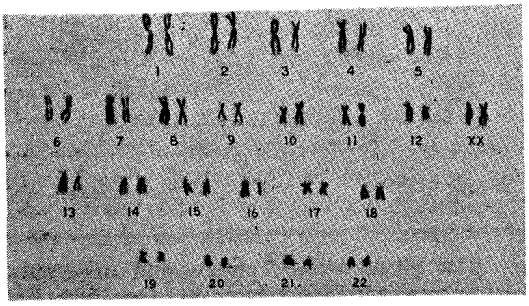


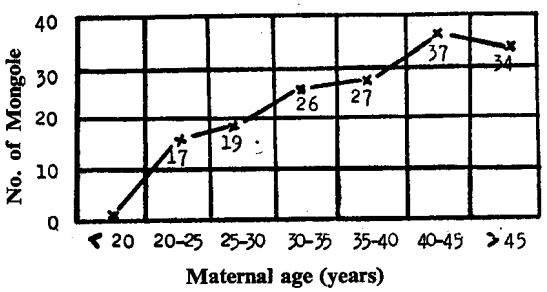

**Fig 9. Karyotype of regular mongol, trisomy-21.**

The condition is due to non-disjunction at meiosis or mitosis and the parents'

**TABLE 4: Mongolism**

| Year | Chinese | Malays | Indians | Male | Female | Total |
|---|---|---|---|---|---|---|
| 1961 | 24 | 2 | 5 | 14 | 17 | 31 |
| 1962 | 35 | 7 | 1 | 19 | 24 | 43 |
| 1963 | 28 | 1 | 10 | 18 | 21 | 39 |
| Total: | 87 | 10 | 16 | 51 | 62 | 113 |

chromosomes are normal, and this is called the regular mongol. However, there are some Mongols who have 46 chromosomes instead of 47 possessed by the regular Mongol, but an abnormal chromosome 15 which actually consists of a translocated 21 and a normal 15, making it finally 47 chromosomes with trisomy-21. This is called a 15-21 translocation Mongol, and hence one of the parents will have the abnormal chromosome 15 which may be transmitted to the offspring. The chances of getting a Mongol is therefore higher in the translocated type than in the regular variety. In the regular Mongol, it has been shown that it is more liable to occur at late maternal ages. Fig 10 shows the distribution of maternal ages at the birth of the Mongol child.




*e* **Talipes:**

By this is meant club feet of various types but of such a severity that they need correction by adhesive plaster or plaster of paris. The distribution for this deformity is shown in Table 5:

**TABLE 5: Talipes**

| | |
|---|---|
| Chinese - - - - | 128 |
| Malays - - - - | 18 |
| Indians - - - - | 29 |
| Males - - - - | 78 |
| Females - - - - | 97 |
| Total: - - - - | 175 |

The overall incidence works out at *1.3 per thousand* which compares with a figure of *2.42 per thousand* in Melbourne (Pitt, 1962). There seems to be a slight increase in the incidence in Indian infants.

*f.* **Natal and neonatal teeth:**

These conditions are associated with premature sprouting of the primary dentition; natal teeth when they are visible at birth and neonatal teeth when the tooth is present at birth under a gum swelling (Wong, 1962). At that time Wong stated that the incidence was estimated at 0.3 per thousand in Singapore but he considered this an underestimate as it was partly a retrospective study. For the years 1962 and 1963, a planned survey was carried out and Table 6 gives the distribution and incidence:

**TABLE 6: Natal and Neonatal Teeth**

| | Chinese | | Malays | | Indians | | Eurasians | | Male | | Female | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | NN | N | NN | N | NN | N | NN | N | NN | N | NN |
| 1962 | 23 | 19 | 5 | 2 | 0 | 2 | 0 | 0 | 15 | 10 | 13 | 13 |
| 1963 | 8 | 26 | 1 | 6 | 0 | 3 | 1 | 1 | 3 | 15 | 7 | 21 |
| Total: | 31 | 45 | 6 | 8 | 0 | 5 | 1 | 1 | 18 | 25 | 20 | 34 |

**TABLE 7: Natal and Neonatal Incidence**

| Place | Quote | Incidence |
|---|---|---|
| Paris Maternity Hospital | Ballantyne (1897) | 0.16 per thousand |
| Birmingham | Hawkins (1935) | 0.10 ,, ,, |
| Cook County | Massler and Savara (1950) | 0.66 ,, ,, |
| Presbyterian Hospital | ,, ,, ,, ,, | 0.55 ,, ,, |
| Hong Kong | Allwright (1958) | 0.30 ,, ,, |
| Singapore | Wong (1964) | 1.12 ,, ,, |

The total number of cases was 97 for the 2 years and this worked out at *1.12 per thousand* which makes it very much commoner in Singapore than elsewhere as Table 7 shows:

The causes for this is difficult to find. It cannot just be due to enthusiasm in detecting the condition because the abnormality is obvious enough not to be missed. The high incidence in Singapore may be tied up in some way with the nutritional diet of the mother because it is very rarely seen in paying-class patients.

*g.* **Multiple Congenital Deformities:**

By multiple congenital deformities is meant deformities which are usually more than five and although it is difficult to describe them as a group yet this group is usually understood by the attending doctor. The incidence is shown in Table 8:

There is no difference in the racial distribution because the number of Chinese infants delivered in K.K.H. is approximately 7 times more than the Malays and 9 times more than the Indians. However, among these multiple congenital deformities, there are some with definite clinical features which mark them out as belonging to one of two syndromes, namely the 13-15 trisomy syndrome and the 17-18 trisomy syndrome. In these 2 conditions, the infants possess 47 instead of 46 chromosomes; the extra chromosome in the 13-15 trisomy being in the 13-15 group, and the 17-18 trisomy being in the 17-18 group, although most workers tend to agree that the extra chromosome belongs to the 18 group.

**TABLE 8: Multiple Congenital Deformities**

| Year | Chinese | Malays | Indians | Male | Female | Total |
|---|---|---|---|---|---|---|
| 1961 | 4 | 1 | 1 | 1 | 5 | 6 |
| 1962 | 6 | 0 | 0 | 3 | 3 | 6 |
| 1963 | 2 | 1 | 0 | 1 | 2 | 3 |
| Total: | 12 | 2 | 1 | 5 | 10 | 15 |

the 13-15 group, and the 17-18 trisomy being in the 17-18 group, although most workers tend to agree that the extra chromosome belongs to the 18 group.

**1. The 17-18 Trisomy:**

Examples of this condition in the local population has been described by Wong and Chua (1963) and consist of prominent occiput, low set ears, micrognathus, typical posture of the hands with index and little fingers covering the others. Often there is a simian crease in the palms. The head protrudes backwards giving the appearance of a rocker-bottom chair (Fig.7):

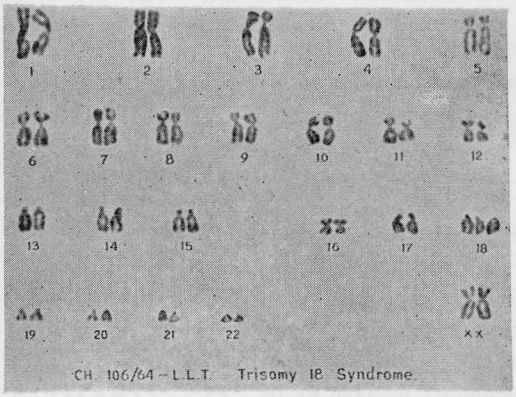



**Fig. 10. Karyotype of 17-18 trisomy. Total chorosomes of 47 instead of 46 with 3 in group 18, instead of 2.**

Fig. 10 illustrates the chromosome constitution with a total of 47 instead of 46, and the extra chromosome being in the 18 group. The cause of this condition is most probably a non-disjunction of the 18 chromosome during meiosis.

**2. The 13-15 Trisomy:**

The first example of this condition encountered in the local population in Singapore was also described by Wong and Chua (1964) and the infant has many of the features of the 17-18 trisomy, such as low set ears, peculiar position of the fingers, rocker-bottom feet; but in addition they have a median cleft lip, microphthalmus and many of the other cases described in America also had skin haemangioma. (Fig.8) Another case has recently been encountered here. Fig.11 shows the karyotype.

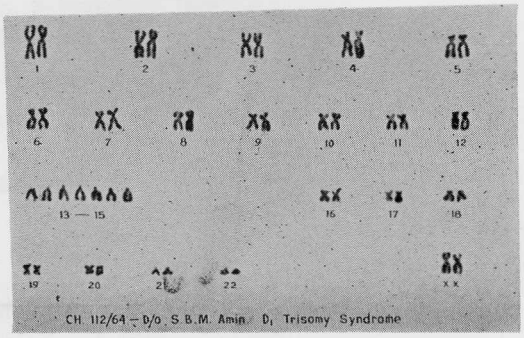



**Fig. 11. Karyotype of 13-15 trisomy. Note that there are 7 chromosomes in the group 13-15, instead of 6 normally, making a total of 47 chromosomes, instead of 46.**

In both these autosomal trisomies, at autopsy, there may be other associated congenital defects such as congenital heart, abnormal renal tracts, and in 13-15 trisomy, the brain often does not show the median fissure dividing the forebrain into 2 hemispheres and the olfactory bulbs are absent. The chromosome constitution of the parents of both these types of trisomies have been normal.

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