CONGENITAL TRANSVERSE DEFECTS OF LIMBS AND DIGITS*

('INTRAUTERINE AMPUTATION')

BY

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Intrauterine amputation of the extremities is an uncommon and peculiar congenital deformity which is characterized by the absence of one or more distal limb portions. Termination of the proximal part is usually abrupt and bears no apparent relation to anatomical boundaries. The term 'amputation' suggests separation, by mechanical force, of a limb already formed rather than a failure of development, but such a view of the pathogenesis of this abnormality is far from universally accepted. It would probably be better to use a neutral term such as 'transverse defects', but for the conservatism of medical nomenclature.

Circular grooves around the digits or limbs, and similar soft tissue defects, also known as ring constrictions, are seen usually in association with 'intrauterine amputation', but also on their own. Here again, there is no agreement regarding the aetiology but, whatever it is, there can be little doubt about the relation of these circumferential soft tissue lesions to transverse defects of the bones.

Little or no information on this subject is found in textbooks of general pathology, obstetrics or paediatrics. References to other cases are scanty and hard to find, but there is really a great wealth of bibliographic material. A helpful introduction to the history of the problem and to other reported accounts is given by Lennon (1947).

Interest in congenital deformities is age-old, but had been focused for a long time on the more spectacular and awe-inspiring monstrosities. Defects of digits and limbs that look similar to those caused by accidents or deliberate wounding or, indeed, the surgeon's knife were hardly considered interesting by the teratologists of antiquity and Renaissance times.

Thomas Bartholin of Copenhagen (1616-1680) is said to be the first to mention a congenitally deficient extremity. He lived at the very threshold of the modern scientific era and belonged to a family well known for their contributions to medicine and biology: Thomas Bartholin's son, Caspar Secundus, was the first to describe the vestibulo-vaginal glands. Thomas was a man of great learning and wide interests (Rhodes, 1957). His textbook on anatomy was translated into English and used widely for a long time. Bartholin's descriptions of monsters, however, tend to be more imaginative than factual (Hendry and Kohler, 1956). The essay which contains a reference to limb defects bears the title 'Gravidarum Imaginatio' and there, in passing, he tells us of a deformed male infant with only one hand and a club-foot. This sounds credible enough: we shall hear more of the combination of talipes and intrauterine amputation. Bartholin goes on to say that the infant's mother, the wife of a respectable citizen of Copenhagen, had been impressed during her pregnancy by the sight of a maimed beggar—perhaps a crippled soldier—with one hand cut off and a lame foot, 'cuius speciem nec die nec nocte potuit oblivisci' (1673).

The next work in which I found congenital limb defects mentioned is Albrecht von Haller's Elementa Physiologiae (1766); numerous case reports by other authors are quoted, and it appears that there had been a great deal of discussion on the theme of 'intrauterine amputation'. Haller himself is sceptical about the 'amputation' aetiology, because the severed portion had never been found—an objection that even nowadays may still be heard. This objection was answered only a few years later by a case report in which the missing portion was actually present, though badly shrunken (Schaeffer, 1775). Here again, 'impressions' were blamed.

So far, these early reports were all written in Latin. In 1791 Samuel Thomas Soemmerring, Professor of

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Anatomy in Mainz, published a work on malformations which was written in German; in this, he included an illustration of a foetus with multiple severe malformations, who had also mutilated digits and constriction rings. Some small sheets of membrane seemed to be adherent to the circular lesions. In the description of this case the author deals with the major developmental abnormalities and makes no comment on the extremital lesions.

The first case report in French, I believe, was published in 1812 by F. Chaussier, Professor and Chief Physician at the Hospice de la Maternité in Paris. The earliest available record of a case observed in this country is that of Watkinson (1825), an obscure practitioner in Soho, whose initials are not even known. His case history, however, is clear and brief, and its authenticity is underlined by the fact that the body of the infant and the severed foot were shown to the editors of the London Medical and Physical Journal, who appended a drawing of the specimen to the article.

The idea that amniotic bands, by interfering with the blood supply, cause ischaemic necrosis of an extremity and eventual separation, should be credited to Montgomery (1832; 1833). What amniotic bands are, and how they may arise, will be discussed later. Defects alleged to be caused by them were included in the large group of 'amniotic malformations'.

It is worth remembering that, in the past, disorders of amniotic membrane and amniotic fluid were held to account for many congenital abnormalities. This concept may have arisen from observation of certain malformations, such as anencephaly, iniencephaly and oesophageal atresia, which are regularly associated with polyhydramnios, while on the other hand sirenomelia, renal aplasia and congenital urethral obstruction are almost invariably accompanied by oligohydramnios. Nowadays we regard excess or lack of amniotic fluid as an effect of foetal malformation rather than its cause. However, it is not to be denied that both oligohydramnios and polyhydramnios may in turn affect the foetus.

As knowledge of malformations accumulated, a more critical attitude was taken with regard to their causation. New information came from the practice of experimental teratology and from the young science of genetics. Amniotic malformations fell into disrepute.

By the time Ballantyne wrote Manual of Antenatal Pathology and Hygiene (1902, 1904) the problem of congenital limb deficiency seemed to be involved and controversial. Numerous observations, interpretations and opinions were critically reviewed by the author, who himself took a reserved view. Ballantyne also mentioned a not so well-known tropical disease called Ainhum which affects adults and is characterized by ulceration and eventual demarcation of portions of extremities. Some authors, including Jeannel (1886), had suggested that 'spontaneous amputations' were caused by foetal Ainhum, i.e. a prenatal degenerative disease.

The degenerative theory was further developed by postulating a primary inferiority of certain localized tissues. This line of thinking found its sharpest expression in a paper by Streeter (1930) who rejected the aetiological significance of amniotic bands and similar structures, and went so far as to deny the significance of any intrauterine traumatic process in the causation of deformities. His views were widely accepted, especially by embryologists, e.g. Sir Arthur Keith (1940), but were opposed by many pathologists, and in particular by Georg Gruber (1939), a teratologist of great experience. Gruber produced some well-documented observations in support of traumatic aetiology in a limited group of transverse defects, but at the same time rejected the primitive mechanistic approach to the whole field of extremital malformation that still lingered.

Gradually it had become apparent that no single theory of causation could explain all lesions labelled as 'intrauterine amputation', and the concept was put forward that some of these cases were due to exogenous, others to endogenous, causes. Birch-Jensen (1949) applied this division in his survey of extremital deficiencies in Denmark.

Edith Potter (1952) accepts this classification and proposes practical criteria for each of the two categories; these criteria will be applied in the interpretation of the present findings and will be discussed more fully later on. On the question of aetiology, Potter concludes that 'the cause of exogenous spontaneous amputation is unknown', but 'the fact that it is occasionally possible to make out attachment of such abnormal extremities to the amnion at the time of delivery, gives support to the idea of amniotic abnormality as an aetiological agent for this particular malformation'.

There are limitations to the useful application of this dualistic theory of causation; but it is none the less more in harmony with observed facts than any attempt to account for all extremital defects by a single aetiological hypothesis.

Few relevant publications have appeared in this country during the postwar period. Eckstein and Eckstein (1946) described a newborn infant with multiple circular constrictions that were successfully corrected by plastic surgery; no obstetric data are
given in this report. On the question of aetiology, the authors accept Streeter’s view.

Lennon (1947) presents a stimulating historical review which vividly recaptures the atmosphere of controversy, and records four cases of his own observation. One of the four infants had skin defects only. Of the other three, two were of exogenous type, while the remaining one had a bilaterally symmetrical absence of one digit and should therefore be regarded as endogenous, but this distinction is not made by the author. The reader is left with the impression that, in Lennon’s opinion, the causative factor of transverse defects in general is amniotic bands; they are demonstrated in one of the four cases. Summarizing the views of other authors, Lennon is able to quote no fewer than 10 different theories of causation. Not all these theories, however, are mutually exclusive, and in some instances, at least, similar views are hidden behind different terminology.

Browne (1957) discussed the pathology of congenital ring constriction in a paper to the British Association of Paediatric Surgeons and pointed out the aetiological importance of retracting ruptured membranes.

Morison (1952) briefly mentions the subject of localized deformities in which the bone tissue itself appears normal and states that ‘intrauterine amputation by amniotic bands or adhesions, or by other mechanical constriction’ cannot explain localized skeletal anomalies’.

Willis (1958) accepts Streeter’s thesis, but believes that deformities can be caused by intrauterine mechanical forces.

Macgregor (1960) expresses the view that ‘the absence of the distal portion of one or more limbs is not necessarily due to a developmental error . . . in some cases this is the result of a spontaneous intrauterine amputation. . . . The cause of the amputation is uncertain, but there is evidence that abnormalities of the amnion may be responsible, amniotic bands causing constriction and finally separation of the part distal to the stricture’.

Quite recently the problem of congenital ring constriction and its complications has been reviewed by Patterson (1961), a plastic surgeon, whose studies are based on the records of 52 hitherto unpublished cases, including 34 of his own observation. In accordance with Streeter, Patterson considers ring constriction to be due to a primary degenerative process of developmental origin, but refrains from being dogmatic.

In the following pages, four cases of transverse defects of limbs or digits are presented, illustrating various aspects of this complex problem.

**CASE REPORTS**

**Case I**

**Mother’s History.** The mother, aged 30, a normally developed woman of Maltese extraction, was admitted in the 37th week of her third pregnancy to the Birmingham Maternity Hospital (under the care of Mr. A. L. Deacon) as an emergency case because of ante-partum haemorrhage.

Her own family history (as distinct from her husband’s) and her medical, surgical and menstrual history were unremarkable. She had an abortion four years ago and a full-term normal delivery one year ago.

The present pregnancy had been complicated by persistent vomiting from the early weeks and by ankle swelling during the last fortnight. On the day of admission, the patient had a sudden brisk vaginal loss of about half a pint (about 250 ml.) of bright red blood, followed by a few irregular vague abdominal pains.

Clinical examination showed no medical abnormality. Obstetrically, the abdomen was found to be large in relation to the calculated length of gestation, while a rather small foetal head was palpated; this suggested the possibility of a twin pregnancy, which was subsequently confirmed by radiographic examination.

On the following day she was still losing small amounts of blood but had no pain. As the bleeding stopped, and placenta praevia could be excluded, she was allowed to go home on the eighth day after admission.

She was readmitted in labour on the day of expected confinement. She had a very slight show; the membranes were intact and remained so, until after 14 hours of labour the cervix was fully dilated. Then an artificial rupture of membranes was carried out, and after a short second stage, the first twin was delivered by the vertex. After this, the second bag of water had to be ruptured, and at the end of a further 30 minutes the second twin was born, also by the vertex. Delivery of the placenta followed five minutes later: it is described as a binovular twin placenta, so presumably, was of di-amniotic, di-chorionic type. It was not submitted for pathological examination.

**Infants.** Twin I, a girl weighing 5 lb. 3 oz. (2,350 g.) was in good general condition at birth and remained so. Her left hand was missing, the left forearm terminating at the wrist with two minute nodules protruding from the skin at the point of termination. There was no evidence of recent injury or scar formation. No deformity was found in the other limbs, nor any other significant abnormality anywhere.

Twin II, also a girl, weighed 4 lb. 12 oz. (2,150 g.) at birth and was in less satisfactory condition, though normal in shape. She never picked up and died when 39 hours old. At autopsy, the lungs were found to be consolidated, with massive alveolar haemorrhage, as commonly seen in newborn infants who have died of respiratory failure. Neither skeletal defect nor other developmental abnormality was detected.

During the puerperium the mother went through a period of severe pyrexia which was never fully accounted
for, but she recovered after a few days and was discharged on the sixteenth day, accompanied by her surviving daughter, Susan, who maintained satisfactory progress.

**Follow-up.** Twin I was seen when she was about 2 years old. She had developed well both physically and mentally. She was able to make use of her left arm and hardly seemed to miss the absent hand.

The mother revealed that a paternal uncle of the child had a similar deformity of the right upper limb. This was subsequently confirmed by a visit of the Hospital Almoner to the family's home. The uncle was 31 years old at the time of the visit and one of eight surviving children; all his siblings are normally developed; no malformation is known to have occurred in either parent's families. He was born with his right arm missing from the middle forearm; there are rudiments of four digits at the point of termination.

He is married and works as an arc welder. His deformity is no obstacle in his job and he is described by his sister as 'more capable, swifter and more sure of his movements than any of them . . . he fixes a collar and ties his tie very swiftly.'

Unfortunately, he did not agree to be examined and photographed.

Twin I was seen again when she was nearly 6 years old. She is a charming, intelligent and self-possessed child (Fig. 1). She had been fitted with a prosthesis which she uses skilfully, e.g. for catching a ball, and is not a bit self-conscious about it—on the contrary, she likes to show off. She is making good progress at school, both in sport and in scholastic subjects.

Her elder brother was seen at the same visit; he is normal physically and mentally. The mother has had no further pregnancies.

**Comment.** The distinctive features of the lesions are the 'healed' appearance, a slight degree of tapering of the stump and the presence of two rudimentary digits.

Using Potter's criteria, one should classify this case as 'endogenous amputation'; if the term 'amputation' is considered a paradox in this context, one might label it 'peromelia', in accordance with Gruber (1937).

The endogenous character is confirmed by the striking hereditary history; the finding of two closely similar cases of congenital limb defect in two consecutive generations of one family is most unlikely to be fortuitous. Genetically, the observed facts can be explained in two ways. Presuming the responsible gene to be recessive, one would have to postulate that it occurred in heterozygous form in both parents of our proposita, as well as in both parents of her uncle. No consanguinity is admitted (the mother is Maltese, the father English), so one would have to assume the occurrence of this gene in three unrelated families! Alternatively, if the responsible gene is dominant but of variable penetrance, it would have to be present in the genotype of our proposita's father, who does not show any comparable defect in his phenotype.

The observation of an abnormality in one of binovular twins and not in the other is of course compatible with its genetic aetiology. It is remarkable that the deformed twin survived and developed into an otherwise normal and healthy child, whilst her unaffected twin sister succumbed to the hazards of neonatal age.

The problems of prosthetics and rehabilitation in similar cases are discussed by Aitken and Frantz (1955).

**Case 2**

**Mother's History.** The mother, aged 32, was admitted to the Birmingham Maternity Hospital (under the care of Mr. A. L. Deacon) in the 25th week of her second pregnancy, because of threatened abortion. Her family history and past medical history were non-contributory. Her menses had been regular. She had had one abortion at 14 weeks, about five years ago. Subsequently she had attended the sub-fertility clinic, but defaulted before the investigation was complete.

The patient's present pregnancy had been uncomplicated until, two weeks before admission, she had started to lose blood *per vaginam*. She also had 'menstruation-like' pains.

She was treated in hospital with bed rest and sedation and advised to continue this at home. Subsequently she had occasional vaginal blood loss and a 'trickle of water'. It was clear that her membranes had ruptured prematurely.

She was readmitted at 31 weeks in labour with good contractions, but the foetal heart could not be heard. An assisted breech delivery was carried out, and a living though badly asphyxiated infant was born. The placenta followed in due course.

The puerperium was uneventful.
The Infant (Fig. 2). A female, weighing 3 lb. 5 oz. (1,490 g.) and 15 in. (38 cm.) long was deformed and died after 55 minutes of gasping and cyanosis.

At autopsy multiple defects of the extremities were observed. The left leg terminated abruptly at the lower third. The stump looked raw, with bone slightly protruding from the soft tissue. The right foot showed a marked degree of talipes; there was extensive ulceration with scar formation at the medial aspect of the right leg, corresponding to the site of the lesion of the left leg. There were more or less marked circular constrictions around all the fingers of the left hand, the proximal phalanges being affected. The constriction around the left middle finger was particularly deep and suggested imminent separation. The middle finger of the right hand was 'amputated' at the proximal interphalangeal joint. No other external deformity was noticed.

Internal examination revealed insufficient pulmonary aeration and anoxial haemorrhages in the broncho-alveolar system; in addition, there were petechial haemorrhages on pleurae and epicardium. No developmental abnormality was detected in any of the internal organs. The placenta showed signs of advanced ischaemic degeneration. Some threads of fibrinous matter were observed in relation to the amniotic surface. The membranes were ragged.

Radiological examination of the infant's skeleton did not reveal any bony abnormality apart from the obvious defects.

Histological examination of tissue from the stump did not show any evidence of primary pathological change.

Comment. This infant presents a typical picture of exogenous amputation: multiple lesions, ranging from relatively shallow, circular grooves around digits to complete separation of a leg with a raw and ragged bony stump, though the soft tissue had healed; there were no signs of regeneration. The skin defect on the medial aspect of the right leg is situated so that it can easily have arisen from irritation by the bony amputation stump.

The mother's report of a trickling loss of liquor ever since the episode of threatened abortion at 25 weeks is consistent with the hypothesis which incriminates the free margin of a hole in the amniotic membrane as cause of constriction. The observation that the membranes were ragged and thready lends support to this explanation. On the other hand, an 'amputation stump' is at least as likely to pierce the membranes as a normal extremity.

No trace was found of the missing foot or of the missing finger-tip.

Case 3

Mother's History. Aged 28, she was admitted to the Women's Hospital, Birmingham (under the care of Mr. A. L. Deacon) because of dysmenorrhoea and vaginal discharge for the past three months. She had one normal pregnancy about eight years ago and had never had an abortion.
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11·5 in. (29·5 cm.). Transverse defects of the right hand across the entire metacarpus and of the end phalanx of the right big toe were noticed. No other abnormality of the skeleton was detected, either by gross inspection or by radiological examination; the bone age was found to be consistent with the size of the foetus.

Autopsy, after prolonged fixation, revealed no gross developmental anomaly other than absence of the right umbilical artery, the left one appearing to be normal.

The placenta had a spongy and somewhat hydropic appearance; the umbilical cord inserted in a velamentous fashion, the vessels being 'unprotected' for a distance of about 2 in. (5 cm.). Histological examination revealed signs of placental immaturity in relation to the apparent gestational age: the chorionic villi were evenly covered by plasmodio-trophoblast, and some persistent cytotrophoblast was found occasionally; the stroma of the villi was cellular. The decidua plate could not be identified because of the blurring and disruption of the architecture by haemorrhage. No distinct boundary could be seen between this haemorrhagic area and the wall of the Fallopian tube. The latter showed multiple foci of chronic inflammatory cell infiltration, but no tuberculous lesions were seen.

Comment. This case could be quoted to demonstrate the absurdity of the term 'intrauterine' amputation.

The evidence is not sufficient to classify the defect as either endogenous or exogenous. Developmental malformations, it is true, are more common in ectopic than in orthotopic pregnancy; this consideration would weigh in favour of an endogenous causation, but there is no supporting evidence, apart from a single umbilical artery. This is usually taken as suggestive evidence of malformation elsewhere in the body (Faierman, 1960), but can also be found in otherwise normal infants.

On the other hand, the rent in the sac was of uncertain origin and cannot be admitted as evidence for exogenous causation, nor can the presence of lesions in two limbs, suggestive though it is.

Case 4

Mother's History. The mother was 34 years of age, a healthy West Indian woman, and she first attended the ante-natal clinic (under the care of the late Dr. Elsie Spiegel) at 27 weeks in her third pregnancy. She had had two healthy children before coming to this country and no miscarriages or stillbirths.

Her present pregnancy had proceeded normally apart from an accident which consisted of a blow to the abdomen during the third month. Foetal movements had been felt from the fifth month onwards. The uterus was consistent in size with the duration of amenorrhoea. No complications were diagnosed either at initial examination or at any subsequent attendance. The pregnancy progressed in a satisfactory way, but went on beyond term, with an episode of false labour at 42 weeks. Eventually she was admitted in genuine labour about three weeks after the date of expected delivery. Progress was slow, the first stage lasting 26 hours, and an artificial rupture of the membranes was carried out to aid cervical dilatation. After a second stage of only five minutes,
a living female infant was born. No liquor amnii was discharged at delivery.

The third stage lasted five minutes. The placenta was expelled by fundal pressure and was stated to be normal and complete, but it was not submitted for pathological examination. The membranes were also recorded as being complete.

The Infant. She weighed 6 lb. 4 oz. (2,830 g.) at birth and measured 19 in. (48 cm.); she was in good general condition and cried as soon as the airways were cleared. The skin was dry. The right foot was missing and there was a raw amputation stump just above the right ankle. On the left leg a ring constriction was seen at about the same level as the amputation on the right. The toes on the left side were hypoplastic. There was no trace of the amputated foot nor were any bands seen.

She made good progress and was gaining weight by the time she was discharged from hospital. At the age of 1 month (Fig. 4) she came under the care of Mr. O. T. Mansfield, plastic surgeon, who at a later date carried out a plastic repair of the circular skin defect on the left leg which had been causing oedema of the foot. He also excised the amputation stump on the right so that an artificial limb could be fitted.

Comment. I saw this baby when she was a few days old, by courtesy of Mr. R. B. Parker (under whose obstetric care the mother was delivered), and found the deformity to be of exogenous type. The mother, an intelligent and co-operative woman, told me her story of a blow against the abdomen in early pregnancy, but the mother of any deformed infant is likely to build up a minor accident that occurred in pregnancy as an explanation for the 'mishap'.

The infant's dry skin at birth is, of course, evidence of oligohydramnios (or anhydromnios). Lack of amniotic fluid, in general, is due either to decreased production, e.g. foetal renal aplasia, or to increased disposal of liquor, such as might be caused by premature rupture of membranes or slow leakage which could go unnoticed. The latter possibility would be consistent with a limited membrane rupture caused by a thrust-out extremity.

In contrast to Case 2 of this series, this baby remained in good general health. While in hospital awaiting operation, she was found to have a moderate degree of anaemia which responded to routine treatment. In the course of investigation she was found to be a heterozygous carrier of the sickle cell trait; this finding has no apparent bearing on our problem.

DISCUSSION

Distinction of Endogenous and Exogenous Defects

This is based on criteria given by Potter (1952). 'The principal exogenous malformations are those in which some part of the upper or lower extremity ends abruptly, usually with evidence of scarring at the terminal point. Such abnormalities are often multiple, different extremities being involved to a different degree. They are also frequently associated with linear depressions that completely encircle one or more digits or the forearm or leg, less often the upper arm or thigh...'

According to Edith Potter, an 'amputation' should only be regarded as exogenous if the remaining skeleton shows no developmental or other abnormality that can be causally associated with it. Any abnormality of the osseous system as a whole suggests endogenous causation. Any apparent attempts at regeneration of the missing portion are also incompatible with exogenous pathogenesis. Furthermore, 'all bilaterally symmetrical abnormalities and those in which the abnormality consists of an excessive number of parts are endogenous'.

These points of differentiation are useful in the interpretation of the morphological features observed and allow us to classify most cases at least tentatively. There are cases that cannot be readily put into one group or another, such as Case 3 in this series. Moreover, these criteria represent only the morphological manifestations of two kinds of causal factor; the nature of these factors and their mode of action are only vaguely envisaged.

The meaning of the terms 'endogenous' and 'exogenous' may vary from author to author. Potter does not define the precise meaning which she attaches to these terms. Dissenting from
Gruber's (1937) interpretation, I suggest that the term 'endogenous' in this context should not be limited to genetically conditioned deformities, but should be extended to imply faulty development of the extremities from any causes that are known to produce true congenital malformations in general, either spontaneously or experimentally. Present-day knowledge of the aetiology of congenital malformations is reviewed by Haring and Lewis (1961) and by Krone (1961). The known causes of disordered development, in addition to faulty genes, inherited or mutational, include chromosomal aberrations and a variety of environmental factors, such as infection, especially by viruses, damage by cytotoxic drugs and other poisons, hormonal influences, maternal deficiency states, hypoxidosis from various causes, actinic damage, variations of temperature, inadequate nidation of the ovum and others. Some of these are known to produce abnormalities indistinguishable from well-recognized hereditary malformations, so-called phaenocopies (Warkany, 1947).

There can be no hard and fast line between endogenous 'amputation' and other developmental abnormalities of the extremal skeleton, such as peromelia, hemimelia and amelia.

Exogenous extremal defects, on the other hand, affect limbs that are more or less fully formed, regardless of whether the mutilating lesions are caused by amniotic constriction and/or other intra-uterine mechanical interference, or have resulted from any other cause, including even 'focal tissue deficiency'.

Where a well-defined developmental anomaly exists in addition to a transverse defect of uncertain origin, one would be inclined to regard the extremal lesion as endogenous. But this inclination need not always be justified: unequivocal exogenous lesions can occur in association with obvious developmental malformations (Ballantyne, 1904; Kohler, 1957).

Another difficulty in separating endogenous and exogenous malformation exists in the possibility that the exogenous cause of a deformity may be a maternal malformation of endogenous origin. This thought had been expressed by Gruber (1937).

'The attempt, generally to divide all malformations of the extremities into those caused by exogenous influences and those due to endogenous—and that means by and large inherited—causes, cannot be pursued to its conclusion: in the individual case, one may be unable to ascertain whether manifest mechanical obstacles to intrauterine growth and development of the foetus are not, in fact, rooted in the maternal constitution.' Earlier, Schwalbe (1906) had formulated a similar idea. 'Many authors claim to have achieved a mechanical explanation of a deformity having demonstrated, more or less plausibly, its causation by amniotic anomalies; the nature of these amniotic anomalies, however, is left to the realm of obscurity.' In the wider field of congenital abnormalities, interaction and interdependence of hereditary and environmental causes has been found in many instances (Stevenson, 1961).

Positive Hereditary History. This is, admittedly, the most unequivocal evidence of the endogenous nature of an 'amputation'. Other endogenous causes are usually difficult to prove in the individual human case—with the possible exception of virus disease. The absence of a hereditary history, on the other hand, does not exclude a genetic aetiology. A variety of reasons may account for the lack of manifestations in other members of the family tree; to discuss these in full is a task for a geneticist.

Insufficient or inaccurate information is the chief obstacle to the genetic interpretation of many an affected family. This is shown strikingly in the well-known case of the 'hand- and footless Brazilian brothers'. Their picture (Fig. 5) has been reproduced in many relevant publications, but with captions differing as regards the relationship of those depicted: the oldest male had been stated to be either the father or a paternal uncle of the other affected members. According to Koehler (1936), who re-checked the available information, this individual is, in fact, the eldest son of the elderly woman who is seen in this picture—care-worn but free from deformity. The father, who is not shown here, is also unaffected. Consanguinity of the parents is admitted: according to their own statement they are uncle and niece, according to local gossip, brother and sister. Whichever is correct, a recessive gene might be responsible, and this would be the simplest explanation. The deformity was present in all male offspring, and also in one of several daughters, so it does not appear to be sex-linked.

Point of Teratogenic Determination of Developmental Malformation

This occurs about the end of the eighth week when the extremities have acquired their gross shape. Endogenous defects, one must assume, originate before that date.

There is no unanimity regarding the gestational age at which exogenous defects arise. Streeter (1930), who postulates a primary circumscribed tissue deficiency, believes that the affected areas become necrotic during embryonal, or early post-embryonal life. 'It is found that in specimens under
20 weeks, the process of amputation is in its active stages.'

Various critical times have been suggested by those authors who admit the possibility of amniotic causation: Ehnhardt (1956) believes that amniotic folds bring about their effect between the fifth and seventh week. Potter (1952) depicts a case of constriction of the digits by a band in a foetus of 10 weeks (Fig. 592, p. 533). R. Torpin (personal communication), on the other hand, thinks that rupture of the amnion, which initiates the traumatic process, occurs in these cases 'months or weeks before delivery'.

The gestational time at which constriction is supposed to occur thus varies within wide limits, and the interval between constriction and demarcation is likewise variable. Browne (1957) has actually observed postnatal separation of a congenitally constricted extremity, and similar observations are recorded by Cleisz and Bret (1948) and by Scheffner (1959).

History of External Trauma

This has been reported in at least three cases in the literature (Martin, 1850; Chiari, 1911; Meyer and Cummins, 1941), in the second case of J. Sakula (personal communication) and also in Case 4 of the present series. The idea that mechanical injury to the mother's abdomen may cause foetal abnormality dates back to Hippocrates (as quoted by Ballantyne, 1904). Mechanical disturbance to the ovum has been used widely and successfully in the experimental production of malformations. One might expect it also to be a cause of disturbed development in human foetuses, but Willis (1958) considers 'it extremely improbable that early mammalian embryos ever suffer malformation from external trauma or compression'. External trauma acting at a later stage causing separation or destruction of limbs already formed is feasible but unproven.

Scepticism regarding the significance, in a retrospective history, of past trauma has been expressed in my comment on Case 4. The mind of a lay person seeks for an explanation of congenital deformity no less anxiously than the physician's mind. Trauma offers too ready an explanation for a lesion, which, by its very morphology, suggests mechanical interference.*

My reservations do not apply to the reports by Meyer and Cummins and by Sakula. In both instances the mothers had been victims of traffic accidents and had been left unconscious, so these two cases are outstanding by both the objective evidence and the extraordinary severity of the trauma.

Possible Causes of Trauma Within Uterus

Here one is faced with the problem of 'amniotic bands'. The nature of these bands has been under discussion since Montgomery (1832) published his paper. Confusion has arisen because various authors (and occasionally the same author) have given this term more than one meaning and applied it to different structures.

The following types of amniotic bands can be discerned:

1. Tissue bridges between amnion and foetus or between two different points of the amniotic membrane. Probably it was this type of band that was looked upon as post-inflammatory adhesion—comparable to pleural or peritoneal bands. Whether inflammation in fact ever plays a part in their formation is dubious, though the idea has been revived by Moell (1948) and by Cody and Uetzmann (1957). Oligohydramnios has also been incriminated as a cause of band formation. Grosser (1939) suggests faulty cavitation of the embryo as one possible cause, and persistence of certain cells of the magma reticulare as another; these magma cells normally become liquefied and absorbed, but occasionally they may persist and form strands. This type of band would, therefore, have to be regarded as a malformation of the amnion, and indeed may occur in conjunction with foetal malformation of developmental origin.

2. Threads of necrotic tissue, sometimes resembling the vitelline cords of hen's egg; the nature of

* Years before I became interested in the study of this anomaly, my wife (A. Kohler, personal communication), when attending an infant's welfare clinic, met a child with a transverse defect of the fingers of one hand; the mother swore that this was due to an accident during her pregnancy when she jammed her own fingers in a door.
these structures is difficult to define. They might well have been taken for solidified lymph by early authors. Occasionally they are seen within circular grooves or in close relation to them, and by their position suggest that they are the constricting agent (Lennon’s Fig. 1). It is this type of band that Streeter probably had in mind when speaking of ‘structures that have frequently been mistaken for amniotic bands’, and he considered these as ‘either macerated sheets of epidermis or strands of hyalinised fibrous tissue which are the residue of the localised areas of defective tissue’.

The possibility that these threads are degeneration products of the structures discussed under 1. and 3. should be seriously considered.

3. Shreds of torn foetal membranes, spurs, pedicles, etc. This type of band is not mentioned by Streeter, yet it is the one most likely to have a traumatic effect. The serious significance of these torn-off shreds has been shown in several well-documented cases where they have caused strangulation of the umbilical cord, resulting in foetal death (Braun, 1854; Moell, 1948; Duncan, 1953; Craven and Geddes, 1953; Cody and Uetzmann, 1957; Kotz and Vidone, 1959).

4. The term ‘amniotic bands’ can be applied with some justification also, to the free margin of a hole in the membrane that had been pierced by an extremity: the membrane may then retract and constrict the thrust-out limb or digit. This is, according to Browne (1957) and R. Torpin (personal communication), the mode in which the amniotic membrane exerts its traumatic effect. A record of early rupture of membranes, of a trickling loss of liquor or of oligohydramnios at birth gives additional support to the claims of these two authors. Extra amniotic pregnancy would represent an extreme example of retraction (Hückel, 1936).

One could also extend the use of the term ‘amniotic bands’ to the ‘cutting edge’ of the neck of an amniotic pouch, such as described by Turner (1960).

In the preceding four paragraphs, the term ‘amniotic bands’ is used to describe structures that are thought to be part of the amnion or of the secundines, and are considered, rightly or wrongly, as aetiological agents. Turner (1960), however, uses the term to denote a foetal lesion, namely, the circular grooves or constriction rings. Even more liable to be misunderstood is the term ‘congenital constricting band’, as applied to the skin lesion by Blackfield and Hause (1951).

Herbut (1953), who misquotes Lennon’s survey, is a victim of this confusion and also makes it more confounded: Lennon lists 10 different theories relating to the aetiology of transverse lesions, including amputation by amniotic bands, and discusses their pathogenesis. Herbut quotes eight of these theories as though they applied to the causation of the bands themselves in a chapter headed: ‘Foetal Membranes’.

It would help if authors of future descriptive reports stated exactly what type of amniotic band they have in mind.

Whether all the various types of bands and similar structures mentioned are capable of causing traumatic constriction, I do not know, but there is no way of denying that fatal strangulation of the umbilical cord can be, and has been, caused by ‘disposed’ portion of membrane. Having accepted this, I can see no difficulty in envisaging constrictive lesions of extremities being caused in a similar way. Moell (1948) has actually demonstrated the simultaneous constriction of umbilical cord and of digits by amniotic bands in a convincing way: less convincing is his explanation of the causation of bands by maternal gonorrhoea. That separation is the ultimate stage of constriction—so clearly demonstrated in Case 2—need not be debated.

No case in this series actually did show membrane attached to the foetal lesion when examined, but I have seen this in one stillborn foetus (by courtesy of Dr. A. H. Cameron): histological examination confirmed the amniotic nature of the sheets of tissue encircling the big toe.

**Significance of Congenital Ulceration**

Skin defects other than ’ring constriction’ have sometimes been recorded in association with intrauterine amputation. In Case 2 of the present series, a fairly large irregular area of ulceration is seen on the medial aspect of the unaffected leg. It is suggested that the sharp and jagged amputation stump has, by constant irritation, caused necrosis and sloughing of the skin, but this explanation may not hold good for all such cases. According to Ballantyne (1902) ‘they find an explanation in the tearing through of amniotic bands during the process of parturition’. Lennon (1947), apparently prompted by Ballantyne, included in his series an infant with skin defects but no other congenital lesion. No supporting evidence for the suggested aetiology was put forward in this case.

D. Browne (personal communication) speaks in this context, of ‘pressure sores’ which he has found in several newborn infants, not only in the extremities, but also on the head and trunk. In one instance at least, they were caused during labour by a cervical contraction ring.
Missing Limb

An objection frequently made to the concept of mechanical severance of an extremity is the failure of most authors to find any evidence of the distal limb portions. Chaussier (1812), Watkinson (1825) and Martin (1850) are among those who have actually found the amputated part. More recently Milew (1936) has briefly described and illustrated a case.

Missing Head

Ehrhardt's observation (1956) is not only unique but also highly relevant to our subject and merits discussion. A macerated foetus (Fig. 6) was born at 41½ weeks, decapitate, but otherwise normally shaped, save for bilateral talipes. Foetal membranes had ruptured at 31 weeks! Foetal heart sounds were audible until eight days before delivery, when they suddenly ceased. At birth, no trace of the head was found. The placenta was not examined by the author, a pathologist, who, at autopsy, found all internal organs normally developed, altered only by the effects of maceration. The normal size of the adrenal glands was emphasized. In spite of these findings, Ehrhardt believes that decapitation occurred during embryonal development. The present reviewer is inclined to attach more importance to the premature rupture of the membranes.

Dysplasia Foetalis

This is the name given to localized tissue abnormality which, according to Streeter (1930), leads to circular necrosis and eventual separation of the distal portions of the extremities: 'Somewhere between not being able to develop at all and the development of abnormal form, is another variety of defective development and, ... it is this type of defective development that results in intra-uterine amputation. In these cases sharply defined areas of limb-bud tissue are of such inferior quality that only imperfect histogenesis occurs. Whether injured in some way or defective from the outset, and the latter is probably true, these areas maintain themselves only in the earlier weeks of pregnancy.'

Streeter himself must have felt the vagueness of this theory, for he prefaces it with an apologetic remark that 'a negative statement regarding the cause of intra-uterine amputation can be phrased more easily and definitely than an affirmative one, stating just why and how it occurs'.

Streeter's thesis is based on the admirably thorough examination of 16 cases, i.e. museum specimens that form part of the Carnegie collection, but his records of the clinical history of the relevant pregnancy are often sketchy, uninformative or altogether missing. He concludes that 'no evidence...
has been found that intra-uterine amputation is due to amniotic bands or adhesions or other mechanical constriction. Amniotic bands do exist and are sometimes associated with malformation, but where this occurs the two participate in the same disturbance, and the latter are not mechanically produced by the former. Streeter’s rejection of amniotic aetiology might have been a reaction against the uncritical generalization of the amniotic theory; but this generalization had been discredited since the turn of the century (Ballantyne, 1904; Schwalbe, 1906).

Owing to Streeter’s great authority, especially among embryologists, his theory has been widely and uncritically accepted; in some textbooks of embryology his opinions on extremital defects—both negative and positive—are presented as though they were proven facts. My intention is not to deny the possible significance of constitutional tissue inferiority or of 'spontaneous' amputation, but to state that relevant and convincing evidence has yet to be produced. The apparent conclusion that the problem has been solved has been a deterrent rather than a stimulant for further thought and research on the subject.

**Experimental Production of Transverse Defects**

This has been achieved in many ways. Bors (1925, 1927) and Nicholas (1926) have tied, *in utero*, the foetal extremities of laboratory animals with silk; this was followed in due course by typical intrauterine 'amputation'. Jost (1953a, b) reported intrauterine demarcation of limbs in the litter of rats that had been given either 'pitressin' (vaso-pressin) or adrenalin. Wooley and Cole (1938) have observed constriction and eventual separation of the tail of the offspring of Norway rats of certain strains, following controlled dietary restriction during gestation. Other strains did not show this mutilation, nor did it appear in a susceptible strain if the mothers were kept on a full diet; so it seemed that both hereditary and environmental factors were involved in the causation of this deformity. Greene and Saxton (1939) succeeded in breeding a strain of rabbits with extremital defects as a recessive Mendelian character: lesions were preceded by vascular disorders and resulted in demarcation.

While these results of animal experiments suggest possibilities in the pathogenesis of the anomalies under discussion, they cannot be directly applied to the elucidation of the problem as it exists in human beings.

**SUMMARY AND CONCLUSION**

This paper is based on the clinical, radiological and pathological records of four cases of congenital transverse defects of extremities—three live-born infants and one foetus of 24 weeks gestational age. Case 1 is classified as an endogenous defect with a relevant hereditary history; the child is of school age now and making good progress; Cases 2 and 4 are examples of exogenous intrauterine amputation; in the former the infant died very soon after birth, in the latter, the infant is surviving. Case 3, the foetus of a secondary abdominal pregnancy, cannot be classified with certainty as either endogenous or exogenous.

The division of transverse extremal defects into those of endogenous and of exogenous causation helps our understanding of the problem; the criteria must not be applied too rigidly, and there are cases which cannot be classified. Endogenous defects are considered to be true developmental malformations. With regards to exogenous defects, the theory of amnio-genic amputation, far from having been 'explained into complete oblivion' (Blackfield and Hause, 1951), is still in the centre of discussion. This theory receives qualified support by the evidence presented in two case reports as well as by the findings of other authors reviewed in this article. Further critical study with careful observations, especially in the field of clinical obstetrics, is needed to find out the exact how and why. Any attempt to 'solve' this problem by just denying its existence is a retrogressive step.

It is a pleasant duty to record my thanks to the clinical consultants, whose names are given in the text, for permission to use case notes of patients under their care. For permission to reproduce Figs. 5 and 6 I am obliged to publishers and authors; for the photographs illustrating my case reports I owe thanks to various friends.

To Professor Georg Gruber of Gottingen, I am deeply indebted for sending me a photostat copy of Soemmering's description and drawing of a monster. I am equally grateful to Sir Denis Browne for his stimulating interest and for permitting me to quote from a personal communication. Similarly, Professor Richard Torpin of Augusta, Georgia, U.S.A., Dr. Jack Sakula of Central Middlesex Hospital, London, and my wife have provided me with valuable, hitherto unpublished information, which I gratefully acknowledge.

I owe thanks to numerous colleagues, senior and junior, clinicians and pathologists who, by discussing the problems of this article with me—and usually by disagreeing—helped me to clarify and formulate my own views; I cannot name them all, but I would like to acknowledge the help given by Dr. C. W. Taylor and Dr. A. H. Cameron.

Last, but not least, I would like to record my indebtedness to Miss Margaret Russell, M.A., Librarian, Birmingham Medical School, and to her assistants; to Miss W. E. Gates and Miss Shirley Simons—past and present Almoner respectively at the Birmingham Maternity Hospital—and to Miss Bette Wheelwright my secretary.
...Amputation of the foetus in utero, with an attempt to explain the occasional cause of its production. Dublin J. Obstet. and Gynæc. Sci., 1, 140. (1833.) Further observations on spontaneous amputation of the limbs of the foetus in utero. ibid., 2, 49. (Available at the Royal College of Surgeons, London.)


Soemmerring, S. Th. (1791). Abbildungen und Beschreibungen einiger Missgeburten. Mainz. (Available at Göttingen, photo-stat copy kindly supplied by Professor G. B. Gruber. Also at the British Museum.)


Watson, C. (1825). Case of a foetus, in which the left foot was separated from the leg during utero-estation. London med. phys. J., 54, 38. (Available at Birmingham Medical School Library, and at the Royal College of Surgeons, London.)


Addendum

After submission of the typescript, I succeeded, thanks to the kind help of Dr. Walter Pagel, in tracing a source referred to by Haller (op. cit.) that had so far eluded me. J. B. van Helmont (1577-1644) mentions in his Orthus Medicinae (edited by his son, F. M. van Helmont, 1652, Amsterdam, apud Ludovicum Elzevirum) on page 478 under the heading 'De Injectis Materialibus' (Tractatus de morbis, No. 14) several instances of limb defects in infants. One of these, a girl, survived into adulthood and married. All these cases of deformity were supposed to be due to 'impression' on the pregnant mother caused by the sight of cripples.
Most fascinating is the story of the birth of a decapitate infant (with a bleeding neck!) to a woman, who was watching public executions of rebels against the Spanish overlords.

Helmont marshals these examples to support the theory of teratogenesis by maternal impression, which was prevalent until the end of the eighteenth century. The description of the mutilated infants is not detailed enough to allow critical appraisal. It appears that Ehrhardt's case (1956) is the only observation of 'spontaneous' intrauterine decapitation that is sufficiently documented. (Helmont's *Ortus Medicinae* is available at Birmingham Medical School Library and so is an English translation of this work under the title 'Oriatrike or Physick Refined'.)
Congenital Transverse Defects of Limbs and Digits: (‘Intrauterine Amputation’)

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