FANTASIES, FACTS AND FOETUSES

THE INTERPLAY OF FANCY AND REASON IN TERATOLOGY

by

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THE publicity surrounding the 'thalidomide disaster'[1] made the year 1962 notable for embryologists. Their subject, previously of absorbing interest only to a select band of dedicated devotees, was thrust into the limelight and embryology's relevance to clinical medicine was exposed for all to see.

Before the thalidomide misfortune a number of clinical factors had begun to focus attention on the study of prenatal development. First from N. W. Gregg's work came the realization that the rubella virus could have a teratogenic effect. Then advances in cardiac surgery stimulated interest in congenital cardiac defects. More recently it has become evident that progestagens given to pregnant women can have a masculinizing effect on the female foetus. Cytogenetic techniques have also catalysed great interest in sexual differentiation and in maldevelopment of the urogenital system.

The greater awareness of the unsolved problems of congenital malformations has been accompanied by a reminder that a pregnant woman in this country seems to have a 1 in 50 chance of producing a grossly malformed baby. Also the realization has come belatedly that it may be unwise to administer drugs to pregnant women, unless it becomes absolutely necessary. Even though medical science is beginning to throw light on the causes of congenital malformations, the natural reaction of anyone closely concerned with the birth of a monster may well be to ask: 'Oh! why did this have to happen?' In fact, this very question seems to have exercised men's minds from earliest times.

It would be a gross simplification of the facts of history to postulate that the initial run of superstitious interpretations were interrupted by the more scientific speculations of the Greeks, only to be resumed in mediaeval times; that superstition gave way to an interest in monstrosities fostered by the commercialization of curiosity and that at last the nineteenth century saw the gradual development of a science termed teratology. Some such vague general pattern may be discernible, but different ages have produced a blend of superstition with philosophical and scientific thought. Superstition was by no means unknown in the classic era; some scholastics of mediaeval times produced some inspired scientific thought. Although the nineteenth century produced men such as P. T. Barnum,[2] the 'King of Showmen' who exploited public curiosity, 'this extraordinary Yankee lived to see the rise of scientific institutions which replaced the catch-all curiosity museums of earlier decades'. This age also produced descriptive scientists of the calibre of Taruffi,[3] who compiled a most detailed account of teratology with extensive discussions of the aetiology and of

the history of ideas related to the subject. Who can say that interest in monsters is entirely scientific in the twentieth century; that superstition is dead; that commercialism no longer succeeds in titillating the curiosity of a fair-attending public? In addition, views which were dismissed a few years ago as rank superstition may have to be re-examined in the light of modern physiology. Maternal stress is now known to be capable of affecting the foetus[4] and evidence has been produced as recently as 1959 to show that reproductive physiology may not be completely uninfluenced by lunar periodicity.[5]

It is difficult to trace any progressive evolution of ideas concerning the problem of teratogenesis and, in order to bring some order into a most confused and intricate aspect of history, the various views concerning teratogenesis will be considered, not in any chronological order, but under the headings:

1. Supernatural causes
2. Astrological influences
3. Seminal and menstrual factors
4. Hybridity
5. Mental impressions
6. Philosophical and scientific explanations

1. *Supernatural causes*

(a) *Divine.* It appears that in the earliest ages monstrous infants were regarded as divine, and the mummy of an anencephalic baby exhumed from the necropolis of Hermopolis is considered by archaeologists to indicate quite clearly that it was worshipped.[6]

Teratology can be invoked to explain the appearances of many heathen gods and demi-gods. The Siren might be a sympodial foetus, the Centaur an infant born with two pairs of lower limbs or a hydrocephalic calf, the Gorgon head an acormic placental parasite, Atlas a case of occipital encephalocoele, Janus a diprosopous monstrosity, and Prometheus, with his liver being torn by the vulture, an instance of foetal exomphalos.

Next came a line of thought making the gods creators of monstrous infants, their purpose being amusement. Pliny only slightly altered the idea and stated that Nature creates monsters for the purpose of astonishing us and amusing herself.[7] Traces of this old belief are still to be found in the use of the word *Sport* in Botany, *Spielart* and *Naturspiel* in German, *jeu de nature* in French and *lusus naturae* in Latin. *Freak of nature* conveys a somewhat similar idea.[8]

Later the notion of sportive, pleasure-loving deities gave way to a graver concept. The purpose of the gods was to warn. It may be that the Latin *monere*, to warn, gave rise to our word monster.

The birth of a deformed infant came to be looked upon as a divine warning, and the deity had to be propitiated to avert some calamity. From this belief to the destruction of the monster is but a step. The Greeks of Sparta may have thrown their malformed infants into an abyss so as to preserve the physical character of the race, but elsewhere the killing was mostly sacrificial and propitiatory, and the mother only rarely escaped the fate of her baby.

Later the idea of deities causing monstrosities became lost in the consideration of the calamity which the phenomenal birth was supposed to portend. Thus

another possible origin of the word monster may be the Latin *monstrare*, to show, or as Cicero puts it: '*Monstra, Ostenta, Portenta, Prodigia appellantur, quoniam monstrant, ostendunt, portendunt, praedicant.*'[9]

A catalogue of monstrosities and the events they predicted was found among the ruins of ancient Babylon. The predictions in this system might be fortunate or catastrophic, and the abnormalities described are certainly capable of being identified by present-day teratologists.

Livy tells us that many an abnormal birth has influenced the decisions of the Roman Senate and Saint Augustine relates how the birth of a two-headed monster in Constantinople during the reign of Theodosius was looked upon as a sign from Heaven, indicating approval of the projected division of the Empire.[6]

Notwithstanding some active opposition on the part of such writers as Fortunatus Licetus and Polydore Virgil, the idea that monstrous births predicted disaster held its ground till the close of the seventeenth century.[10]

Some records of the Renaissance period show how strong this belief was and they make most entertaining reading.

Conrad Wolffhart, in 1557, described many monsters. The most astounding of all appears to have been the 'terrible child' who was

> born in Craconia of noble parents, who was indeed most terrible to behold. It had bright fiery eyes, the mouth and nostrils like an oxes. It had long hornes and a black hairy fur like a doggs, and on its breasts faces like apes.
>
> It further had the heads of doggs on both elbows looking backwards, and at the whirl-bones of each knee, looking forward.
>
> It was splay-footed and splay-handed. . . . It was born and lived four hours, and spake thus: 'Watch, the Lord our God comes!' The author adds naively: 'But these are things related only upon the credit of some particular writer and may, like Popish traditions, be or not be believed.[11]

It is, however, characteristic of this period that monsters and indeed other abnormal beings came to be patronized rather than shunned and were received at the various courts of Europe.

John Bulwer, in the mid-seventeenth century, wrote:

> But we must know above all things, that these apparitions that be contrarie to nature, happen not without the providence of Almighty God, but for the punishing and admonishing of men, these things by just judgment are often permitted, not but that man hath a great hand in these monstrosities.

Talking of compensatory aptitudes of congenital defectives he adds:

> Nature upon such occasions is, that her unsearchable industry as it with great wittinesse appeareth everywhere, yet more eminently in those bodies wherein as t'were unmindful of her charge or business she hath frustrated of this or that number, which errour as it were, with some shamefac'dness she abundantly recompenceth by a munificent liberality.[12]

(b) *Satanic influence.* It was inevitable that the concept of a beneficient Deity permitting the occurrence of monsters, or indeed sending them as a chastisement, should sooner or later be complemented by a special brand of satanic teratogenesis. And so it was that in the Middle Ages, the devil and the malign

influence of his emissaries came to be blamed for the birth of monstrous and malformed infants. Happy and lucky the mother of a monster, when there was found a preponderance of evidence in favour of the stellar origin of her abnormal progeny, otherwise she would hardly escape death by burning, she and her 'devil's brat'.[13]

Only the more unsightly monsters were believed to be engendered by Satanic seed, but should hideous features be present, they proclaimed to all and sundry that the paternity was of the worst and shadiest.[14] One wonders how many an unfortunate woman perished in flames, convicted and convinced by such over-riding evidence—evidence which could only mean that she had succumbed to the wiles of the Infernal Seducer!

Belief in the evil eye is linked with fear of demons and demonic possession. It had its origin in the dim past before the beginning of historical records and is found among many different peoples. Long after its inception, the belief was given specious support by the theory of vision evolved by the Greek philosophers. They taught that visual rays were thrown out by the eye to strike external objects, from which the rays were reflected back to the eye. Thus vision was a form of energy originating in the eye of the observer. Belief in the power of the evil eye persisted till the end of the last century and women were required to take thought of the dangers attendant upon pregnancy and childbirth, when the evil eye might seek her out to cause the birth of a monstrosity. The danger of the evil eye was considered to increase as pregnancy advanced.[15]

2. *Astrological causes*

The positions, movements and combinations of the heavenly bodies have had a profound influence on the opinions and beliefs of ancient races concerning the origin of terrestrial phenomena. The Chaldeans were, as is well-known, past-masters in the art of divination from all kinds of phenomena, stellar or terrestrial. That they connected teratological and astrological occurrences is also beyond doubt. There is abundant evidence in the official records of the Chaldean astrologers of 2800 B.C. that the birth of a malformed baby was treated as an event of grave import.[16] Twentieth-century man cannot nor indeed wishes to abandon a sneaking regard for such beliefs.

The development of astrology with the casting of horoscopes led the practitioners of that ancient art to attach the utmost importance to the birth of anything abnormal, either human or animal. These phenomena were regarded as the result of astral positions at the time of the birth, and the monstrosities were taken to be reflections of the heavens, on which all terrestrial things depended. Thus the abnormality foretold the future with as much certainty as did the stars and the planets.

When a hermaphrodite is born, the son of the palace shall rule the land.

When a woman gives birth to an infant: that has the ears of a lion; there will be a powerful king in the Country. . . .

That has a bird's beak; the Country will be peaceful. . . .

That has no mouth; the mistress of the house will die. . . .

Fig. 1

The barber who had neither hands nor feet. The extent to which this man overcame his disabilities is illustrated by the small pictures: he can play dice, write, sharpen a pen, play a xylophone, load a gun, shave himself, carve in wood, play skittles, empty his pockets, shuffle cards, thread a needle, sketch

From Saltarino, *Abnormitäten*, Düsseldorf, Lintz, 1900

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Fig. 2
From a playbill in the Wellcome Collection

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That has no feet; the canals of the Country will be cut and the house ruined.
That has no nose; affliction will seize upon the Country and the master of the house will die.
Whose anus is closed; the Country will suffer from want of nourishment.[17]

It emerges from these records that special auguries were drawn from births to royal personages, and twins in particular were regarded as portending good fortune to the king and his country.[18]

Ptolemaeus Claudius, an Alexandrian astrologer of the second century, not only stated the astral conditions under which monsters were born, but also mentioned the nature of the malformations to be expected. The position of Venus, or of the moon, at the moment of conception came to be considered as having a potent effect in determining whether the infant was to be normal or malformed.[19] About the year 1200, a cow gave birth to a deformed calf, said to be half human. The cowherd in charge thereof, being suspected of an unnatural crime, was condemned to be burned at the stake. Luckily for him, Albertus Magnus pointed out that the teratological phenomenon might be due to a particular constellation and so the cowherd's life was spared.[20]

It is only fair to point out that Albertus, a saintly Dominican Friar, was, on the whole, inclined to treat the suggestion of astrological influences on foetal life with considerable scepticism and reintroduced to Europe the philosophical concepts of ancient Greece. So with Needham we may say: 'Albertus, rightly called Magnus, has had the happy fate of being beatified by the Church and by Science'.[21]

Eclipses have frequently been endowed with instantaneous teratogenic powers, and Rueff, in 1585, observed that 'in Sicily there happened a great eclipse of the sun and immediately many deformed and double-headed children were born.'[22]

In a work entitled *Grande Encyclopédie Universelle*, by Henricus Asteldius, published in the seventeenth century, it is stated that a Danish astronomer, who was also a medical man, had discovered the origin of monstrosities. He ascribed them to comets, which he regarded as tumours scattered throughout the firmament and which, when they were precipitated upon the earth, took on there all kinds of unusual and extraordinary forms.[23]

Among the heavenly bodies the moon has always held a high place in popular esteem as regards her effect upon mundane affairs. Even today one still meets otherwise fairly enlightened people who believe the moon has a profound physiological effect upon conception and sex-determination. The coincidence of a twenty-eight day cycle for both the female and the heavenly body is obviously too much of a good thing for the popular mind. Nevertheless on a more scientific plane Menaker and Menaker[5] drew attention in 1959 to the fact that the concept of a twenty-eight day lunar month is fallacious, the mean synodic lunar month (i.e. new moon to new moon) being 29·53 days long. They present evidence showing 'a small but statistically significant synodic lunar (or sun-moon) influence on the human birth rate, and presumably on the conception rate and, perhaps, on the ovulation rate'. In view of this it may be more prudent not to dismiss as entirely ridiculous the time-honoured belief in

lunar teratogenic powers. The term 'moon-calf' is witness to this belief and it is well to recall that Shakespeare uses it on several occasions in the *Tempest* when referring to Caliban, 'a freckled whelp, hag-born—not honoured with a human shape'.

3. *Seminal and menstrual causes of teratogenesis*

The theory that monstrous infants are the result of variations of the paternal element in generation is a very old one and seems to have been first expressed by Empedocles of Agrigentum in Sicily (495–435 B.C.). He has been called the 'Father of the Evolution idea'[24] and seems to have had some knowledge of embryology and teratology. He thought that monsters happened either from abundance or from defect of the semen, from slowness or aberration of its movement, or from division of it into several parts.

Democritus of Abdera, at about the same time, thought that double monsters were generated when the semen belonging to one or two species was introduced into the uterus repeatedly at intervals. To begin with, the first ejaculate reached the womb and sufficed to form the new being; soon thereafter the second volume of semen arrived and began to operate in its turn, and so limbs and organs came to be duplicated. The abuse of coitus was thus made out to be a teratogenic factor.[25]

Neither Empedocles nor Democritus ascribed to the female any formative power in the matter of generation. To them she was only a specialised and complicated incubator! Aristotle, on the other hand, believed that the mother contributed to the substance of the zygote and, in consequence, his theory of teratogenesis included somewhat similar faults in the female element as well as in the semen.

Galen, however, living in the second century A.D., seems to have believed in a purely seminal theory. He thought that hermaphrodites were due to the entrance into the uterus of spermatic fluid from both testicles, one testis producing males, the other females.[26]

The idea, that the menses play an important part in the generation of monsters, seems largely to have been the result of the Hebrew legislation regarding coitus during and immediately after the flow. Also, the deformed Vulcan is said to have been begotten by Jupiter when Juno was menstruating.[27]

Avicenna, an Arabian physician of the Dark Ages, believed that semen deposited in the left side of the uterus gave rise to a girl and in the right side to a boy. When placed in the middle of the womb it led to the procreation of a hermaphrodite.[26]

Though the Middle Ages were darkened by ideas of supernatural and astrological teratogenesis, Albertus Magnus, the Dominican monk and bishop mentioned earlier, accepted with modifications the views of the Greeks. He resembled Aristotle in considering at length the phenomena of generation and he speaks of the origin of monsters. He divides into four the modes of corruption of eggs: (1) decomposition of the white; (2) decomposition of the yolk; (3) bursting of the yolk membrane, and (4) *antiquitas ovi*.[28] Had St. Albert suspected

that man also develops from an egg, we might have been enlightened by some mediaeval views concerning the relation of maternal age to the incidence of congenital malformations, not to mention an anticipation of Professor Witschi's views[29] concerning maldifferentiation of sex.

4. *Hybridity as a cause of teratogenesis*

The wise men of old saw little reason for according less credence to a fourth mode of producing monsters, namely 'the mixing of seeds'. If mortals could have affairs with gods which yielded a superhuman progeniture, why should not intercourse with animals be blamed for the production of monsters, which were considered to be only half-human? Thus, Plutarch implies that Thales accounted for centaurs in this way,[30] and traces of similar notions are to be found in the mythology of many races.

It is easily understood how such beliefs arose when it is remembered that at the time all kinds of animals, including man, were reputed to be fertile with one another. Our mediaeval cathedrals are full of carved representations of the results of imaginary unions twixt fur, feather, scale, hoof, claw and fin. What more picturesque than the clandestine rendezvous of a cock and a viper to account for the basilisk? In more recent times M. de Réaumur pondered over the strange love of the hen for the rabbit and conjectured whether it would bring forth a hairy chick or a feathered rabbit.[31]

Not till the beginning of the eighteenth century was an effective protest made against the notion of hybridity explaining teratogenesis. Bianchi pointed out in 1741 that when the product of human gestation had a rough resemblance to an animal form, the resemblance might be due to foetal disease.[32] All the same Ballantyne could still write at the very beginning of the present century: 'Even at the present day however, there still exists a strong popular belief in the old theory and even in the ranks of the profession I have met with its adherents.'[33]

5. *The teratogenic effect of mental impressions*

The belief in the potency of maternal imagination on the development of the foetus is as old and as widespread as the human race. Who can say that the idea is dead today? A striking feature of most folkloric explanations of this brand of teratogenesis is that the mental impression is most effective at the time of conception, and indeed it has long been held that any condition prevailing at the moment of conception affects the child. Bastards engendered with supposedly greater passion are commonly thought to be gifted with artistic promptings. It is even recorded that a woman succeeded in establishing the legitimacy of her 'posthumous' child by proving that her husband had eaten fish the night the child was conceived and that the water in which the child had bathed always had a fishy smell.[34] The idea, that the eating of millet seed, mice, or two bananas by married women leads to the conception of twins[35] can be considered under the same heading.

When tracing the more serious aspects of the evolution of the theory, it becomes evident that the earliest record of it is to be found in Genesis. It

recounts the events which establish Jacob as the first experimental embryologist. By placing partly peeled, streaked and mottled rods of poplar, almond and plane trees before the flocks when they conceived at the water-trough, he induced the flocks to bring forth streaked, speckled and spotted lambs and kids. He then put these offspring (instead of the rods) before the flocks and further increased the number of such animals. Finally, in order to get as vigorous a breed as possible, he put the part-peeled rods before only the stronger members of his experimental series as they mated. This secured his prosperity, his father-in-law having promised to leave him all his mottled and speckled lambs and kids.

The Greeks believed that women gave birth to infants resembling the statues which they liked to gaze at during their pregnancy, and Spartan wives were required to look upon representations of the strong and beautiful, e.g. statues of Castor and Pollux.[36]

Pliny imagined that human beings are more unlike one another than other creatures because

> . . . sight, hearing and calling to remembrance; or imaginations only received, and deeply apprehended in the very act of generation, or the instant of conception. The wandering cogitation also and quicke spirits either of father or mother, flying too and fro all on a suddaine, from one thing to another, at the same time is supposed to bee one cause of this impression, that maketh either the foresaid uniform likeness or confusion and variety. For the nimble motions of the spirit, the quicke thoughts, the agilitie of the mind, the variety of discourse in our wits, imprinteth diverse formes, and many markes of sundrie cogitations; whereas the imaginate facultie of other living creatures is unmoveable, and alwaies continueth in one, in all it is alike and the same still in everyone, which causeth them alwaies to engender like to themselves, each one in their severall kind.[37]

Soranus of Ephesus spoke of the apelike children which were born to women, who had looked at monkeys near the time of conception.[38] The colour of Chariclea, the white daughter of the black king and queen of Ethiopia, was explained by the fact that the queen gazed upon a representation of the lily-white Andromeda in the early stages of her pregnancy.[39]

Prior to the fifteenth century the notion was evidently well established in Europe, but it does not seem to have been used to explain the birth of monsters. In the early seventeenth century Gervase Markham made some pertinent comments about the theory[40]

> and scoffs at the superstitions propagated by Gesner and others concerning the predetermination of the colour of the foal by holding something of the desired colour—or even a painting on board or canvas of the foal required—before the mare during conception.
>
> 'Were there a certaintie in such practise, I know so many fantasticall wits in this Nation, that we should not be without a worlde of *Gesners* Horses, I meane horses of all manners of colours in the Rainbow; Nay some madde men I knowe would have their Mistresses names grow on their horses buttockes, but letting these iugling trickes passe, the only sure way to have your foale of good colour, is to have your Horse and your Mare of a good colour, and that doth never faile in nature.'

Despite occasional enlightened statements by men such as Markham, the revival of classical learning in the West fostered such an upsurge of the theory

concerning the influence of maternal fancy, that there seems to have been no limit to the flight of the imagination and its teratogenic potency. Doubtless, the women of that day were glad to welcome the change in outlook, for the substitution of the maternal fancy theory for that of Satanic or bestial intercourse rendered the birth of a malformed foetus a misfortune, but no longer a crime.

By the sixteenth century the concept had become well established in the popular mind and was receiving professional support. Ambroise Paré tells us how Jean Bellanger, surgeon to the King of France, saw a child with a frog's head in the vicinity of Fontainebleau.

> If Magdeleine Sarbourcart, stricken with fever, had not, in order to cure herself according to the advice of a neighbour, held a live frog in her palm at the time her husband was embracing her, she would not have been delivered of a child with a frog's head.[41]

The seventeenth century produced a heavy crop of colourful descriptions of the alleged effect of maternal imagination, and attempts were made to provide a rational basis for the theory. Thus Descartes could be relied upon to reason that: 'The image of a given object is sometimes transmitted by the arteries of a woman to one or other part of the foetus and imprints there, marks known as birth-marks, which provoke the astonishment of the learned.'[42]

In the *Encyclopedia Chirurgica* we find Dolaeus holding that the image in the mind was involuntarily communicated to the animal spirits, which impressed it upon the foetus by means of the nerves of the uterus.[43] The notion was somewhat stultified when Giulio Bandiera of Venice brought in the effect of paternal imagination, which could only act prior to, or at, the time of impregnation.[44]

Robert Boyle, whose mind conceived the well-known Law concerning the relation between volume and pressure, conformed sufficiently to contemporary thought to repeat a tale about a speckled child whose mother had gazed long and earnestly at some red pebble-stones at St. Winifred's Well.[45]

In 1726 the theory that maternal impressions affect the foetus was brought prominently before the public and the profession in England as the result of the notorious case of Mary Tofts and her rabbits.[46]

It is quite likely that this case stirred Blondel to deal the maternal impression theory the most deadly blow it had yet received. In his book *The Strength of Imagination in Pregnant Women Examin'd*, Blondel skilfully arranged his facts and arguments with intent to prove that the current theory was unsupported by experience, by reason, or by anatomy. He concluded that conception, growth and sexual determination of the embryo were all outside the power of the mother's will. 'How,' he said, 'can anybody believe, without reflecting upon the Wisdom of God, that it is left to her to disfigure the child and to spoil the regular Work of Nature?'[47]

Blondel's work had a great effect upon medical opinion all over Europe and soon numbered adherents in nearly every civilized country. Nevertheless the old theory continued to be supported by many authorities and it may be of interest to know that, near the close of the eighteenth century, the monetary value of a maternal impression, of a patriotic kind, was set at four hundred

French francs per annum. Isidore Geoffroy-St.-Hilaire records how, in the third Year of the Republic, an infant was born with the representation of a Phrygian cap of liberty on the left breast, and to the mother the Government of the day awarded the above sum, presumably in recognition of her patriotic thoughts.[48]

By the beginning of the nineteenth century the members of the medical profession either subscribed completely to a belief in the potency of a mother's imagination to make her foetus in exact resemblance with the object acting on her mind, disbelieved in such power, or adhered to an intermediate line of partial acceptance of the doctrine.

It is true that it was becoming increasingly difficult for the trained physician to accept the theory, for the researches of the previous century had demonstrated that there was no direct communication between the circulatory system of the mother and that of the foetus, and at the beginning of the century under consideration it became evident that no demonstration of a structural nervous union was forthcoming. On the other hand, the effect of the anatomical discoveries was to some extent diminished by the enunciation of the concept of animal magnetism by Franz Mesmer and its partial acceptance by the medical profession. If the tenets of this new doctrine were correct, there was no longer any need for the demonstration of nerves in the umbilical cord. The century saw a gradual but steady decline in the number of adherents in Britain to the concept of maternal impressions, and this decline was reflected, after an initial delay, by a similar trend on the Continent. It is somewhat surprising to note that, while this brand of credulity was declining in Europe, there was a marked recrudescence of support for the theory in America, in medical as well as lay circles.[49]

6. *Philosophical and scientific explanations*

Hippocrates, Anaxagoras, Alcmaeon and Menander became interested in avian embryology, and discussed avian teratogenesis in terms of reduplication of the yolk. They seem to have based their theories on the observation of 'an egg provided with a double yolk, from which a chick to some extent double, is observed to arise—that is, with two heads, four legs and the like. . . '.[50]

Aristotle pointed out that when the yolks were separated by a vitelline membrane normal twins resulted, but continuous yolks produced double monsters. He also attempted a purely philosophical explanation of why monsters occurred in nature. To quote again from Adelmann's translation of Fabricius' *Treatises*:

> Whatever Nature makes she makes to serve some purpose . . . making everything because it is necessary or better so. Nature thus belongs to the class of causes which acts for the sake of something (final cause). The end or final cause is prior in reality to the phenomena which leads up to it. The latter, however, are prior in time or order to development.

Aristotle goes on to say that in addition to the final cause, for the sake of which the preceding steps have been taken, Nature must reckon with absolute

or simple necessity which proceeds from the nature of the material she uses. Sometimes this absolute necessity subserves the ends of Nature, or final cause. On the other hand

> absolute necessity may defeat the operation of the final cause, as with monsters. The monstrosity, though not necessary in regard to a final cause and an end, yet is necessary accidentally.
>
> Monstrosities belong to the class of Things Contrary to Nature, not any and every kind of Nature, but Nature in her usual operations; nothing can happen contrary to Nature considered as eternal and necessary.[51]

In addition Hippocrates and Aristotle both considered that deformities might be due to causes acting mechanically upon the foetus. Hippocrates wrote:

> As to the infant crippled in the womb, I say that it is crippled in consequence of a contusion, the mother having been struck on the place corresponding to the foetus, or having had a fall, or having sustained some other form of violence. If the infant experiences a contusion, it becomes crippled in the part contused; if the contusion is greater, the membrane which surrounds it ruptures and the woman aborts. Or yet again infants become crippled in the following way; when in the womb there is a narrowness at the part where in fact the crippling is produced, it is inevitable that the body moving in a narrow place shall be crippled in that part.[52]

This quotation does not refer to monstrosities so much as deformities, such as club foot and congenital dislocations; but it is of great interest as the earliest expression of a belief in the moulding power of the intra-uterine environment.

Aristotle went further than the Hippocratic writers, for he considered, as already mentioned, the reason why and the manner in which true monstrosities were produced. He perceived brilliantly that the cause of a malformation must act during the early period of embryonic life—the period we now know to be devoted mainly to the differentiation of new tissues and organs, and it is precisely while tissues and organs are differentiating that they are particularly susceptible to teratogenic influences. He also used the 'pressure idea' which he inherited from Hippocrates to explain why monstrosities are more common in animals that have several young.

With the revival of interest in the classical authors at the Renaissance, the theories of Hippocrates and Aristotle were aired again, and later commented on and amplified by workers such as Hieronymus Fabricius, his pupil William Harvey, and Nathaniel Highmore.[53] Ambroise Paré has this to say:

> We are constrained to confess by the events of things, that Monsters are bred and caused by the straitness of the Womb; for so Apples growing upon the Trees, if before they come to just ripeness they be put into strait vessels, their growth is hindred. So some Whelps, which Women take delight in, are hindred from any further growth by the littleness of the place where they are kept. [He continues] They which sit idely at home at the time of their being with Child, as cross-legged, those which holding their heads down, do sew or work with the needle, or do any other labour, which press the belly too hard with cloaths, breeches, and swathes, do produce children wry-necked, stooping, crooked and disfigured in their feet, hand and the rest of their joints.[54]

In the seventeenth century monsters were unhesitatingly ascribed to abdominal constriction applied on the part of mothers to conceal their pregnancy. The fact, as L. Schröck pointed out, that women illegitimately pregnant tended to

lace themselves tight to conceal their condition, yet did not seem to produce a greater proportion of monsters, did little to discredit the theory.[55] Though there was a distinct diminution in the popularity of the pressure-theory among medical men, owing to Morgagni's view that foetal diseases were the direct causes of monstrosities, it cannot be said to have died out till this century. By this time the theory had become respectable in its 'Scientific Form', i.e. tight corsets were discounted and the offending factors had become constricting umbilical cords, amniotic bands, irregularities of the uterus, etc.[56]

Alongside the evolution of the pressure-concept, recent centuries have witnessed the growth and passage of several other attempts at a rational interpretation of teratogenic factors and some of these make interesting reading when considered in the light of present day scientific developments. For instance, Ulysses Aldrovandus, born in 1522, suggested most reasonably that monsters come from yolks which are in some way physico-chemically abnormal.[57] Also, in the Baroque period 'light mysticism' led to one development of great interest. Marcus Marci of Kronland, a Bohemian, published a work which was a mixture of purely scientific contributions to optics and speculative theories about embryology. Thus he explained the production of the manifold complexities from the seed in the process of generation, by an analogy with lenses, which will produce complicated beams from a single light source. The formative force radiates from the geometrical centre of the foetal body, creating complexity, but losing nothing of its own power. Monsters originate from accidental doubling of the radiating centre, or from abnormal reflections or refractions at the periphery,[58] surely a brilliant piece of guess-work, anticipating the concepts of present-day experimental embryology regarding field forces, mirror-image reduplication and organizers.

The systematic study of monstrosities, or abnormal formation of animals, may be said to have begun in the first half of the eighteenth century, when Caspar Friedrich Wolff laid the foundations of a rational science and showed it to possess a more than curious interest for the anatomist and the embryologist.[59] He pointed out that, what had formerly been regarded as expressions of influences outside nature, were explicable by the application of definite laws of development, as set forth by embryology, which could form a basis for the classification of malformations.

By the nineteenth century, it had become possible to hatch eggs more or less successfully from furnaces, though the losses were still great. G. Bonnemain and Jouard referred to the large number of monsters produced.[60] In 1809 J. A. Paris wrote:

> During the period that I was at College, the late Sir Busick Harwood, the ingenious Professor of Anatomy in the University of Cambridge, frequently attempted to develop eggs by the heat of his hot bed, but he only raised monsters, a result which he attributed to the unsteady application of the heat.[60]

Thus experimental teratology was off to a good, if unintended, start.

In 1826 Étienne Geoffroy-St.-Hilaire published his work on experimental

teratology,[61] and to him belongs the claim of being the first to experiment upon chicken eggs during incubation. By pricking the embryos through holes in the shell, or by varnishing the shell and thus cutting off the embryo's supply of oxygen, he obtained a large number of anomalies among which were instances of defective heads and spina bifida. We owe it largely to Geoffroy-St.-Hilaire and his son Isidore,[48] that the study and classification of monstrosities and abnormal creatures became recognized as a distinct science in the nineteenth century. They gave this science the name of teratology.

The name of Ambroise Paré has already featured more than once in this survey, and it is fitting that his name should come to mind again at its conclusion. He was the first to attempt classifying congenital malformations and his list of teratogenic causes[62] provides a summary of the theories which have been held in the past and which a modern author would find hard to better:

> There are reckoned up many causes of monsters: the first whereof is the glory of God, that his immense power may be manifested to those which are ignorant of it. . . . Another cause is, that God may punish men's whickednesse, or show signs of punishment at hand. . . . The third cause is, an abundance of seed and overflowing matters. . . . If, on the contrary, the seed be anything deficient in quantity, some or other members will be wanting, or more short and decrepite. . . . The ancients have marked other causes of the generation of monsters . . . the force of imagination hath much power of the infant. . . . Monsters are bred and caused by the straightnesse of the womb . . . by the ill placing of the mother in sitting, lying downe or any other site of the body in the time of her being with child. . . . By the injury of hereditary diseases, infants grow monstrous, for crooke-backt produce crooke-backt, lame produces lame, flat-nosed their like. . . . Monsters are occasioned by the craft and subtlety of the Devill.

In the present century the outlook on congenital malformations has undoubtedly changed. Much more is being done than ever before 'to ensure that each handicapped baby is helped to develop fully to the limit of his potentiality by expert technical aids and "habilitation" methods'.[63] Although in the past many handicapped individuals surmounted their affliction, as is illustrated by the accompanying figure, the 'habilitation' depended very much on the character of the individual and of his close relatives.

How much nearer are we to answering the question: 'Why do monsters occur?'

It is now realized that double monsters are incompletely separated monozygotic twins, the mechanism of their production being explained in terms of incomplete splitting of the organizer region of the embryo, which normally determines the laying down of the embryonic axis. It is generally accepted that abnormal development results, in most instances, from the interaction of hereditary and environmental factors.[64] In a number of instances it has been possible to associate a particular type of malformation with a specific chromosomal defect and the evidence in support of the inherited nature of several abnormalities is overwhelming. However, the exact rôle of genes in normal and abnormal development has not yet been established, but it is considered that they act by elaborating chemical substances, which in turn affect the differentiation and the rate of development. Any alteration in the rate of a developmental process may have considerable repercussions, as the correct timing in

the successive developmental steps is a decisive factor in the control of normal development.

Environmental factors are now known to play a part in the causation of these defects. They are many and varied consisting of such causes as maternal age, order of pregnancy, seasonal, geographical and social factors, blood incompatibilities, maternal dietary deficiencies and maternal infections. As well as chemical agents in the form of drugs taken by the mother, physical agents such as X-rays will affect the development of the foetus and, as was mentioned in the introductory paragraphs, there is now evidence that maternal psychological stress may affect the foetus, possibly as the result of such maternal hormones as adreno-cortico-steroids passing across the placenta.[4,64]

It is thus obvious that progress is being made as regards the elucidation of how malformations occur, but why they should occur is still a question of philosophy.

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