TWINS IN HISTORY AND SCIENCE

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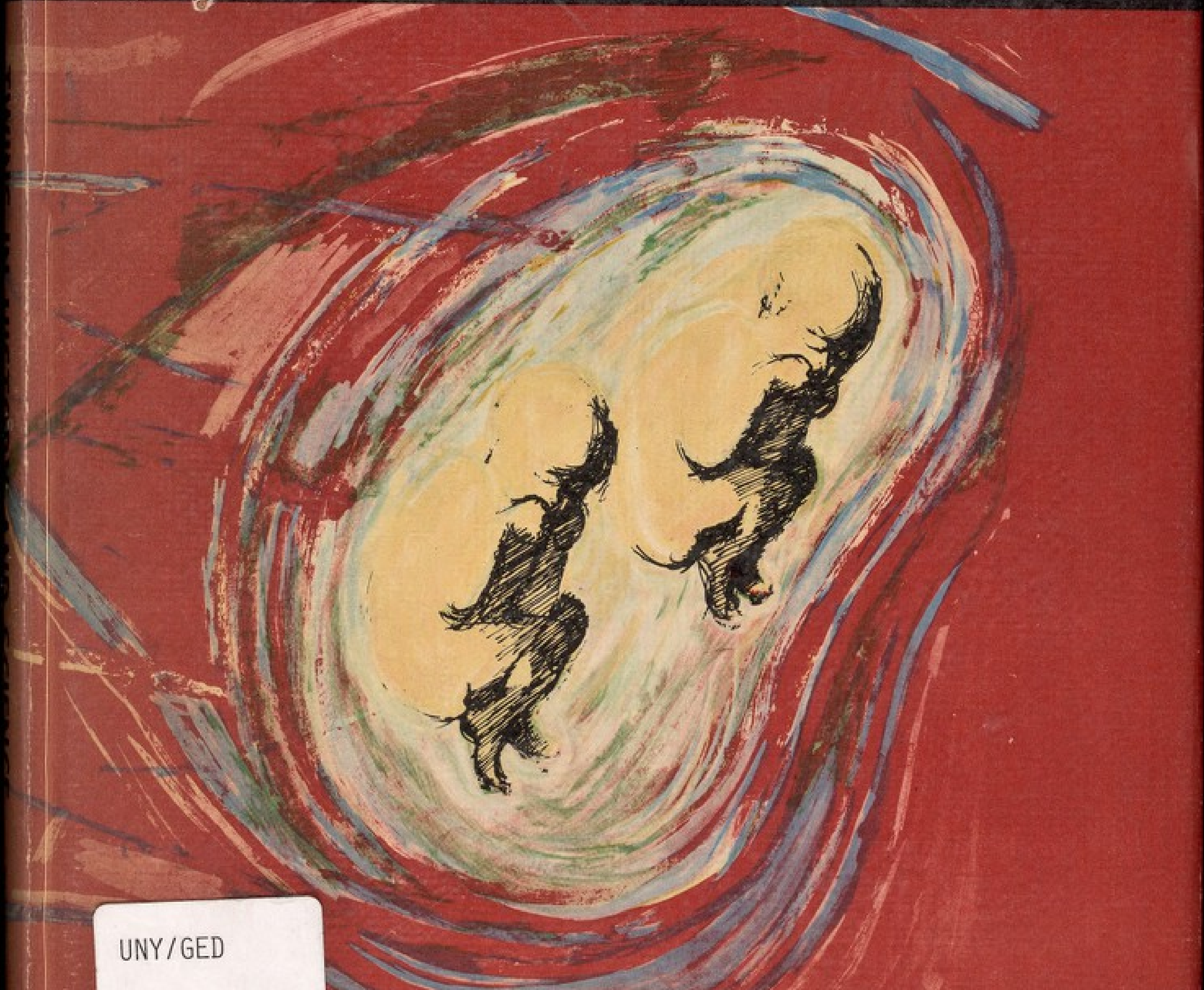

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"Professor Gedda has successfully assembled the world's knowledge of twins and of twinning. He has presented the data completely, he has discussed it authoritatively and he has produced an inspiring book which promises to arouse interest anew in the English speaking world in the subject of twins." - From the Foreword by ROBERT M. STECHER, M.D.

TWINS IN HISTORY AND SCIENCE

The problem of twins as a phenomenon of nature has attracted the attention of poets, writers, artists, sociologists, geneticists, biologists, anatomists, and pathologists throughout the ages. Although much has been written on the subject, this is the FIRST COMPLETE AND COMPREHENSIVE STUDY--a monumental work of amazing size, scope, and scholarship.

The study of twins is of great significance in the development of the knowledge of human heredity. In identical twins, with identical inheritance, the effect of environment can be observed, under controlled conditions. On the other hand, fraternal twins afford opportunity to show differences in inheritance under as nearly identical environmental circumstances as it is possible to provide.

Professor Gedda's study represents a SIGNIFICANT ADVANCE IN THE FRONTIERS OF GENETICS. It is without a doubt a classic in the science of gemelologia.

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Garrison = Morton

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FOREWORD

It is an honor as well as a privilege to be asked to write a Foreword to Professor Luigi Gedda's American edition of *Twins in History and Science*. Having bought *Studio dei Gemelli* when it was published in 1951, there has been ample opportunity to thumb through the 1381 pages, admire the 547 illustrations and study the 161 tables. I have been amazed at the size, the scope and the scholarship of this monumental work. Many of the fine points of this fascinating book have escaped me because my knowledge of the Italian language is limited to a few catch phrases of some of the more popular Italian operas.

My interest in an American edition of *Studio dei Gemelli* was aroused in 1953 when I attended the Dedication Ceremonies of the Istituto di Genetica Medica e Gemellologia "Gregorio Mendel" in Rome. At that time an American translation was under consideration, but final decision was delayed until after the First World Congress of Human Genetics was held in Copenhagen so that the latest information on the subject could be included in the translation.

Some differences will be apparent between the original Italian edition published in 1951 and the present American edition. Besides the introduction of new material, it has been decided to publish the book in two volumes separately. A few of the illustrations have been eliminated to bring the cost of the book within reason, and short selected bibliographies included in each volume. Some idea of the material concerned in the first volume can be gained by reviewing the chapter headings. They are Twins in Mythology and the Arts, History and Science of Twins, Twins in Plant and Animal Life, Frequency of the Twinning Phenomenon, Etiologic Background Factors in Twinning, The Genetics of Twins, Twin Pregnancy and Anatomical Studies of Twins. The two volumes together will discuss thoroughly and authoritatively twins and twinning from every conceivable angle.

The study of twins is of great significance in the development of the knowledge of human heredity. In identical twins, with identical inheritance, the effect of environment can be observed, under controlled conditions. It is amazing to see how different identical twins may become due to accidents in the womb, infection in early childhood and differences in nurture under separate circumstances. It is amazing to see how closely alike are the destinies of identical twins separated in infancy, although often unaware for many years of the other twin's existence, closely alike physically, mentally, emotionally and socially. On the other hand, fraternal twins give opportunity to show differences in inheritance under as nearly identical environmental circumstances as it is possible to provide. Professor Penrose thinks twin studies are not valid because twins are not normal to begin with. It is true, identical twins start with only half a cell and both twins share the facilities and opportunities of one womb and they get only one half of a mother's attention in infancy. These may be limitations, to be sure, but twin studies, the science of gemellologia, have advanced the frontiers of genetics significantly.

Professor Gedda has successfully assembled the world's knowledge of twins and of twinning. He has presented the data completely, he has discussed it authoritatively and he has produced an inspiring book which promises to arouse interest anew in the English speaking world in the subject of twins.

Having been intimately acquainted with the publisher for many years, I know it is no accident that he undertook to produce this excellent set of books, and to make it available in the English language. The subject is of great interest. The book will attract a lot of attention and will have the widespread distribution which it deserves.

ROBERT M. STECHER, M.D.
Cleveland, Ohio

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TWINS IN HISTORY AND SCIENCE

Chapter I

TWINS IN MYTHOLOGY AND THE ARTS

1. TWINS IN MYTH AND FOLKLORE

IN THE HUMAN SPECIES, twins represent a biological rarity, a happening out of the ordinary, arising from the fact that the mother gives birth not only to one new being but to two or more specimens of her kind. So impressive is this exception that it has not failed to leave its mark on the imagination of men of every ethnic group in every epoch of history.

The interest and curiosity aroused by the phenomenon of twinning may be found in ancient mythology where twin divinities are frequently encountered. In the Pantheon of ancient Mesopotamia, for instance, we find Lugalgirra and Meslamtaea, both called Mastabba in Sumerian and Mâsu in Accadan – names meaning "twin." The Babylonian and Assyrian Civilizations were the first to introduce twins in astronomy. There were seven twin constellations, among them the pair Lugalgirra and Meslamtaea, called the Greater Twins.

The use of this expression in the vocabulary of astronomy has been retained from remote times up to this very day, with the constellation of the Twins, which dominates the firmament in the month of May, giving rise to innumerable legends and horoscopes.

Among the Persian divinities are the names of Ormazd and Ahriman, twin sons of Zervan, as well as those deified pairs in the Pantheon of the Helamites described as "make-believe" twins by Furlani.

In Indian mythology, among the celestial divinities of the Vedic faith (the most ancient of Indian religions), great importance was attached to the young twin gods named Aśvin (derived from Aśva, horse, and meaning "the horse owners"). According to the works of Oldemburg and Ballini, these twins were the brothers of Aurora and bridegrooms of the Daughter of the Sun. Inseparable, they were beautiful and strong, as well as learned. Compassionate toward the weak and the oppressed, these god-doctors worked miracles for all who suffered. The old were made young, the blind recovered their sight, cripples were cured, and the wives of the impotent bore children. Rig-Veda contains fifty hymns dedicated to them, and they were invoked three times daily by the Vedic chanter in sacrificial rites.

In Greek mythology the most famous twins are the Dioscuri (from diòs kúroi—sons of Zeus), who strongly resemble the Aśvin Brothers of the Vedic poems. Roscher, C. R. Harris, A. H. Krappe, E. Bethe and others have written about the myth itself and the religious impact of Dioscurism.

Legend hints at mysterious circumstances surrounding the birth of these twins. As some would have it, they were born out of an egg delivered by Leda, wife of Tyndareus. It seems she had been impregnated by Jove, who had taken the form of a swan in order to seduce her.

In another version, Leda produced two eggs, Helen being born from one and the Dioscuri from the other. Then again, it was thought that Pollux and Helen were born from one egg and Castor and Clytemnestra from the other—the first two being considered Jove's and the other two fathered by Tyndareus (Leda's husband).

These disparate interpretations somewhat alter the biological significance of the twin birth (if such it was) of Castor and Pollux. Apart from the introduction into mythology of an oviparous procreation by Jove's turning into a swan, what puzzles us is the suggestion of superfecundation by which the Dioscuri, sons of the same mother, would be offspring of different fathers.

The similarity between the Aśvin Brothers of Indian mythology and the Dioscuri of Greek mythology leads us to believe that the legend may possibly have been derived from an even earlier Indo-European source. Among the Celts and the Germanic peoples a similar pair named Balder and Höder were considered equal to the Dioscuri by Timaeus (*Diodorus*, IV, 56) and Tacitus (*Germ.* 43). It seems certain, at any rate, that Castor and Pollux were regarded in Europe as real Greek gods, an opinion expressed by Varro (*De lingua latina*, V, 66). Homer, Sappho and Simonides were among the many Greek authors who sang of the Dioscuri.

The legend of Castor and Pollux eventually passed into Etruscan and Roman mythology with some changes, the two gods becoming confused with the Penates. Dionysius of Halicarnassus declared he had seen a representation of the Penates in a temple on Mount Velia (Palatine) in the form of two young men in military uniform (I, 68), and a similar representation appeared on a coin belonging to the family of the Sulpicii.

The Dioscuri were commemorated by Horace, and in Cicero we read how they fought with the Romans against the Latins in the battle of Lake Regillus. There are innumerable literary references, and archeological traces, to this pair in classic antiquity. In Italy and Eastern Mediterranean regions the story of the Dioscuri is often interwoven with that of the Khabirs and seems to have derived from Asia Minor. The popularity of the Dioscuri in Rome is reflected in the exclamations "by Pollux! by Castor!" (*Edopel! Mecastor!*), which were part of the speech of the day.

Another twin birth appears in Greek and Latin mythology with Latona giving birth at the same time to Apollo and Diana. Less famous cases of twin births in Greek mythology are those of the winds Calais and Zetes, sons of Boreas and Oreithya; Aedlus and Beotus, sons of Neptune and Menalippe; Eretteus and Bute, sons of Pandion and Zeusippe; Toante and Euneus of Jason and Isophiles; Elatus and Aphidantis of Arcade and a hamadryad; Acrisius and Proetus of Abas and Aglaia. Aesiodus, in his *Theogony*, relates that the nine Muses were born of Jove, the father of the gods, and Mnemosyne (memory), with whom he had lain for nine consecutive nights.

According to the elaborated version by Aesiodus and Euripides of the legend surrounding Hercules, the Greek hero, son of Zeus and Alcmene, was born together with Iphicles, whose father was Amphitryone, a mortal married to Alcmene. Here we find a repetition of the phenomenon of superfecundation encountered in the story of the Dioscuri.

In the XIIth *Canto* of the *Aeneid*, Virgil portrays the Furies as triplet daughters of the Night:

". . . there are two monsters
whose name is Dire; produced
together with the Tartar Megera
in but a single birth, by the deep Night;
She with a serpent's coils did cloak
her babes and arm them well with ventose wings."

(AENEID, XII vv. 1056-1061)

As for the birth of the Minotaur by Pasiphaë, we read in Virgil, "*mixtumque genus prolesque biformis*" (*Aeneid*, VI: v. 25), to which Servius adds, "It is true that in Daedalus' house Pasiphaë slept with Taurus (a notary of Minos) whom she loved, and since she bore two twins, one from Minos and the other from Taurus, it is said that she gave birth to the Minotaur. Therefore the *mixtum genus* is a fact (twins of two fathers) and the *proles biformis* a fable."

The stories in another group of legends in Roman-Greek mythology have in common the theme of twins being abandoned at birth and brought up by shepherds. Such a tale is the one about Amphion and Zethus, children of Jove and Antiope. Having given birth to the twins near Eleutera on the Cithaeron, Antiope left them to their fate. As luck would have it, they were found and cared for by a kindhearted shepherd.

The tale of Neleus and Pelias, twins by Neptune and Tyro, is very similar. Neleus was suckled by a she-dog and Pelias by a mare, and they were subsequently found by some shepherds who brought them up. The same fate befell Licastus and Parrasius, sons of Ares and Philemon, who were abandoned by their parents on Mount Erymanthus, suckled by a she-wolf, and then found by a shepherd named Tilipus.

From a probable adaptation of a Greek fable transposed into Latin mythology, the most famous of all these legends originated —the tale of Romulus and Remus. Sons of one of the Vestal Virgins, these twins were also suckled by a she-wolf. The story goes that Numitor, during a dispute between his shepherds and those of Amulius, recognized the twins as bearing a striking likeness to his unhappy daughter, Rhea Silvia, who had borne twin sons.

The theme of the she-wolf's adoption and suckling of Romulus and Remus is not altogether legendary. We read in Kipling's story about an Indian boy who grew up among wolves. Also, in Gesell's scientific studies (1941) there is a detailed account of how, in 1920, two Indian girls named Kamala and Amala were taken away from the pack of wolves that had reared them. According to Plichet (1949), about a dozen cases have been recorded in which infants were adopted and suckled by wolves, bears and even leopards.

The classic figure of the she-wolf, with Romulus and Remus taking her milk, is quite well known as the emblem of Rome. Indeed, Rome may be said to be the city of twins. Legend has it that Siena was also founded by Remus. In any case, the she-wolf and the twins are the ancient emblems of this town too.

Halfway between legend and history are the triplet brothers Horatii and Curiatii who, according to Titus Livius, were famous in history as heroic defenders of their people. Titus Livius explains what caused the war between the Romans and the Albani during the reign of Tullus Hostilius, and tells about the decision made by the two factions to resolve the issue with as little bloodshed as possible.

All these legends, with the intricate embroidery of their details, reflect the beliefs of those living in remote times. They represent a fantastic and poetic elaboration of the notions primitive people entertained about twins. Furlani has pointed out that there exists among various nations a special religious attitude towards the phenomenon of twinning and twins themselves. As an illustration, we quote the following passages from Tentori's studies of the customs and beliefs about twins among the North American Indian tribes of California:

"In 1922, during a scientific expedition in Southern California, the American ethnologists E. Gifford and R. H. Lowie chanced to come across the survivor of a pair of twins in the territory occupied by the Akwaala tribe. From this twin, who was splendidly attired, Gifford and Lowie learned that it was customary for all twins of that tribe to wear magnificent garb as a mark of distinction for their privileged status.

"Among the Akwaala tribe it is considered a lucky privilege to give birth to twins. The spirits of twins are held to have come to the world from a region called Patcuixa Bue, situated to the south of the Akwaalas among the mountains of Southern California. Some always remain there, while others reach the world through a human mother. Sometimes the accoucheur's persuasive powers succeed, and sometimes not, as he cannot completely impose his will on that of the twins. It may therefore happen that one of the pair dies, or both die.

"These ideas clearly indicate a belief in the existence of the soul before the body. However, Gifford and Lowie did not succeed in finding any notions of supernatural conception in twin births. The father of twins seems to be definitely looked upon as the true father, and his offspring accordingly are mortal.

"Twins also enjoy a special standing among the populations of the Cocopa, Mohave and Yuma. Among the Mohave tribe, twins are supposed to be of supernatural origin and to possess the powers of clairvoyance. 'We have only come to pay you a visit,' they declare. 'Our parents are up there. Let us live with you a while.'

"Not only are Mohave twins favored because of the surprise, admiration and respect that are engendered when the mother gives birth simultaneously to two beings who resemble one another, but also because the event carries with it religious implications and a sense of the supernatural. The Mohave are careful to treat their twins with complete impartiality. They maintain that if more is given to one, the other will grow angry and return whence he came. They also believe that if one twin dies, the other will follow him, even when quite healthy.

"The Cocopa are convinced that twins originate in the heavens, and only come to the world on a visit. If they like their earthly existence they remain, otherwise they return to the heavens. They must therefore be treated with a special regard and affection.

"Among the Yuma twins are also treated with great consideration. Every care is taken of them lest they yearn for their land of origin and die in order to return to it. A Yuman myth concerns an old woman, Akoi Senuxau, who had always avoided men but was raped by a gopher while bathing in a pond. Before returning home, the old woman gave birth to twins. When they had grown to manhood, and after a number of adventures, they were assaulted by a band of Maricopa enemies. The younger one was killed. The other, on seeing his dead brother, collapsed and let himself be killed too. Apparently, the Yuma, like the Cocopa, believe that if one twin dies, his brother will follow him. The Tubatulabal and the Paiute of Surprise Valley are likewise persuaded that there is a uniting link between twins. . . .

"There are no explicit indications of favoring twins in the Diegueno and Luiseno tribes. But there is a myth about these people which tells of the adventures of twins who were conceived in a mysterious way by a woman called Sin-yohauch, daughter of the sky and of the earth, while bathing in a pond. The story shows the almost mystical aura surrounding the birth of twins, as well as their privileged standing. It tells how the two young men, considered nephews of the sky, after various adventures, go in search of twin sisters. One day, the girls suddenly appear before them, attracted by the melodious sounds of their flutes. The brothers have found the two girls at last, but only to be killed in the end by the girls' father.

"Other tribes in California are extremely hostile toward twins. Among the North Pomo and the Kato, both members of a pair are put to death. Often, in the hills of the Northwest Maidus, even the mother is killed. The Wailaki, the Achomaivi, the Yurok, the Miok and the Pitt Rivers content themselves by killing one of the twins.

"Several superstitions support this special kind of infanticide. The North Pomo, for example, believe that twin births are caused by an enemy's malediction, and if the twins were allowed to live they would harm each other. The Yurok's practice is to suffocate one of the twins, generally the female if they are of opposite sex, because they think the two might eventually commit incest. Among the Tolowa tribe, the twins can live if they are of the same sex, but only the first-born may live if they are of opposite sex. The reason for killing the second is perhaps the same as that adopted by the Alsea, who say the second twin is not a real person. According to Powers, the Pitt Rivers kill one of the twins because the burden of two children would be too great.

"Then there are certain tribes who try to explain the phenomenon of twin births on natural grounds. The Northwest Yavapai, for example, say a woman gives birth to twins when, during labor, she lies on her back instead of her side. By so doing, the fetus splits in two, producing two individuals. The Patwin of the hills, on the other hand, maintain that twins are born when the mother overworks herself during pregnancy.

"Twin births rarely occur among the South Maidu. If both babies are suckled by the same mother, each one is always nursed at the same breast. The Wappo have no special ways of treating twins. The River Patwin merely take note of which twin is the elder. The Sinkyon ignore them altogether. No special attention seems to be shown toward twins among the Southeast Yavapai.

"The fact that the twin phenomenon has aroused particular feelings and customs among primitive people can generally be explained psychologically. The ideas held about twins probably derive from the impressions caused by such strange births. How is it there are two children instead of one? The primitive mind explains the phenomenon as being due to the intrusion of some supernatural force. That is why twins assume a special character which can result in a positive or a negative attitude toward them.

"There are certain similarities worth mentioning between the positive attitude toward twins among California tribes and among those in a neighboring region. Beyond the Great Basin in the plains of New Mexico, we find tribes where twins are treated with great consideration. Among the Zuni tribes of the Pueblos population, there are two war gods, twin children of the sun, named A'Hayuta. They are wont to appear in the form of two cruel and disobedient children, hiding their power beneath a mask of obscene and ridiculous mien. They live on mountain tops and are masters of all high places and lords over every kind of dispute. Their worship is in the hands of the priests of the bow, and to this cult are admitted only those who have killed at least one enemy in war.

"The A'Hayuta twins also preside over all games. The reasons why war and sport should be connected in this way are not quite clear, except that a game is like war in that it is played by two or more antagonists, and some of the objects used in sports bear a likeness to certain war weapons. Before using the bow and the spear for hunting and fighting, these men learned as children to manage these weapons in games imitating their elders."

2. TWINS IN COMEDY AND TRAGEDY

As in mythology and poetry, the theme of twins has been used effectively in the theatre. While Greek authors undoubtedly wrote comedies about twins before the Roman comic dramatist Plautus did, the Greek source on which he based his *Menaechmi* has not yet been identified with certainty. In the past it was believed that Plautus' comedy was an imitation of a Greek one written by Epicharmus. Ladewigs, however, maintains that it probably came from a comedy by Posidippus entitled *Didumoi*. Other scholars do not accept this theory.

The twins Plautus brings to the scene are sons of an old merchant of Syracuse. Even as babies these twins were so alike that neither their nurse nor their mother was able to tell them apart. When they were seven years old, the one named Menaechmus was taken to Taranto by his father and accidentally lost in a crowd. He was picked up by a merchant who took him to Epidamnus to live with him, and made him his heir. Time passed and the merchant died. The young man married, but lived in riotous dissipation with a courtesan, Erotia.

Meanwhile, years before, the real father had died of grief. When the grandfather learned the sad news of his lost grandson, he changed the name of the remaining twin, Sosicles, to that of Menaechmus. When this second twin grew up he went in search of his brother. Arriving at Epidamnus he was mistaken for the true Menaechmus. After a series of odd and involved situations arising from their perfect resemblance, the two brothers met and recognized each other on the spot.

Plautus' *Menaechmi* has been translated into many languages, and more or less imitated in a number of European countries. The theme of this perfect resemblance is excellent material for scenes of comedy and drama. The first free imitation is *Calandria* by Angiolo Dovizi da Bibbiena. While the Menaechmi in the Latin comedy are identical male twins, in Dovizi's version the twins, though very much alike in appearance, are a male and female.

Calandria was in turn imitated many times. Among others, the comedy *Gli Ingannati* may be mentioned because of its literary merit. Written by an unknown member of the Academy of the Enthroned of Siena, it, too, had a long series of imitations. It was translated into French under the title *Les Abuses* by Charles Estienne in 1540, summarized and translated in part into English by T. L. Peacock in 1862, and imitated in Spain by Lope de Rueda in the comedy, *Los Engaños*.

Shakespeare in England, perhaps inspired by the fact that he himself was father to twins (Hamnet and Judith) used the twin theme in two of his comedies. The first, written in his youth and greatly resembling the plot of *Menaechmi*, is *The Comedie of Errors*. In it there are two pairs of identical twins all born under the same roof on the same day, with one set being the slaves of the other.

It happens during a shipwreck that each twin is bound to a mast with one of the other pair. They all reach safety but land on different beaches. For twenty years the twins remain separated from each other. When they meet again the usual misleading and confusing situations arise. The physical resemblance between the members of each pair is startling. The author describes the two slave twins as having identical warts and moles, so much so that the lover of one of them claims her rights because she recognizes him by these very markings. The wife of one of the master twins, finding herself face to face with both of them, exclaims, "I see two husbands, or mine eyes deceive me."

Another of Shakespeare's comedies based on the twin theme is *Twelfth Night, Or What You Will*, probably written between 1600 and 1602. The plot resembles that of the Sienese *Anonimo*, but the circumstances leading to the separation of the twins, the locale and the characters portrayed are all different. In what is perhaps the best comedy of its kind, the physical resemblance of the twins, Viola and Sebastian, is absolute. In the fourth scene of the third act Viola says:

> *". . . I my brother know*
> *Yet living in my glasse: even such, and so*
> *In favour was my Brother, and he went*
> *Still in this fashion, colour, ornament,*
> *For him I imitate. . . ."*

The duke with whom Viola is in love, finding himself face to face with the two twins, exclaims: "One face, one voice, one habit, and two persons. A naturall Perspective, that is, and is not" (Act V, Scene I). Sebastian's friend Antonio asks him, "How have you made division of yourselfe? An apple, cleft in two, is not more twin than these two creatures. Which is *Sebastian?*"

The plays in which Shakespeare makes mention of twins have been catalogued by Walsh and Pool.

Goldoni in 1747 wrote a play entitled *I due Gemelli Veneziani*, which was used as a model for later themes, especially in the French theatre. Goldoni is credited with having created and brought to the stage a pair of twins who were psychologically different from each other, unlike earlier writers of comedy who had always conceived of psychologically identical twins, even when they were of opposite sex.

Actually, Goldoni was not the first to adopt this theme, for in 1705 the French writer Regnard told of twin brothers who were identical in appearance but quite different in character in his comedy *Les Ménechmes, ou Les Jumeaux.* These two comedies by Goldoni and Regnard were often imitated. Collalto, the "Pantalone" of the Italian theatre in Paris, took his basic ideas from Goldoni's comedy for a farce entitled *Les trois Jumeaux Vénitiens*, which was translated into German by G. F. Bonin in 1778.

Tristan Bernard's comedy, *The Brighton Twins*, written at the beginning of this century and staged for the first time in 1908, repeats the age-old motif of identical twins. The perfect resemblance is accentuated in this comedy by the fact that each twin is unaware of the existence of the other. On meeting, they think they are dreaming and exclaim, "*Il y a deux moi!*"

In 1839, Victor Hugo did a rough sketch of the plot of a drama about twins to be called *Les Jumeaux*, but never completed it. The story dealt with an unsuccessful attempt to escape on the part of an unhappy political prisoner who, despite lack of proof, was thought to be the twin brother of Louis XIV. For this reason he was captured, imprisoned and ultimately exiled. His face was covered by an iron mask in order to prevent him from usurping the right of succession to the throne of the first-born twin. Subsequently, this plot served as the theme of one of Alexandre Dumas' works.

3. TWINS IN FABLES AND IN FICTION

A Chinese tale concerning identical twins can be found in a collection entitled *Kin-Kon-Ki-Kouan*. These stories were written during the Ming dynasty (1368-1644), translated into French by A. Remusat (1827) and published by É. Legrand (*La Matrone du Pays des Soung. Les deux Jumelles.* Paris, A. Lahure, 1884). The twins, who were born in the province of Hou-Kouang and whose father was Siao-Kiang, were much courted for their beauty and intelligence. Out of the crowd of admirers, it became necessary for the parents to choose two suitable husbands for their daughters. The first attempt to do so ended in a quarrel between the father and mother, and the matter had to be brought before a mandarin.

Finding that the twins disapproved of their parents' choice, he took it upon himself to find husbands for them by announcing a literary competition. Two unmarried writers, Tsin-tsin and Tchi-wen won first prize. However, when it was discovered that Tsin-tsin had written the poem submitted by Tchi-wen a problem arose. Tsin-tsin had already been married twice and both his wives had died. He refused to marry again because the astrologers had warned him never to marry only one wife at a time. The problem was solved when the mandarin decided to let Tsin-tsin marry both twins and have two wives.

Giovanni Boccaccio (1313-1375) in the Twelfth Day of his *Decameron* has Fiammetta telling a story about King Charles of Anjou in which there are twin girls born of a single birth, daughters of Neri degli Uberti. One of them was called Ginevra the beautiful, and the other Isotta the fair.

A fairy tale by the Grimm Brothers, *The Two Brothers* (*Die zwei Brüder*), tells of the adventures of twins who were turned out of their home and befriended by a hunter. Another story about twins by these same authors is entitled *The Golden Babies* (*Die Goldkinder*). In it, two golden twins are born out of two little golden horses, while two golden lilies are in bloom.

George Sand, in her novel *La petite Fadette*, gives a vivid and detailed description of the physical and psychological attributes of the twins, Landro and Silvan. Born when their mother was approaching old age, these twins resemble each other so closely that it is difficult to tell them apart. In order to distinguish the first-born, Silvan, from his brother, a small cross is tattooed on his arm so he may claim the first child's rights of inheritance.

The mother, ridden by prejudices about identical twins, fears that one of hers must die, but the midwife assures her that both will live and be healthy. The father also is afraid. He has heard that a twin's friendship for his brother is so great that if they are separated they do not know how to live, and at least one of them may be so frightened at this idea that he ends by dying of worry. The midwife tries to comfort the father by saying that although his fears are not without foundation there are ways of avoiding such consequences. She advises the parents not to make a habit of keeping the boys together, but rather to let them indulge in separate activities. Also, it would be better not to punish or reprove them together, nor dress them alike. All this advice goes unheeded.

"Landro," wrote the author, "was slightly taller and stronger, had thicker hair, a larger nose and brighter eyes. He also had a wider forehead, a more determined countenance, and a birthmark on his right cheek, while his twin had a much paler one on the left. The villagers could thus tell them apart, though not easily, and at dusk or at a distance nearly everybody was mistaken. Furthermore, the twins had similar voices and, knowing how others would mistake them, they would answer one for the other without saying so. Only their mother was never mistaken, even at night or so far away as to barely see or hear them.

"They were found to share the same tastes in color and once, when their aunt Rosie wanted to give them each a tie for the New Year, they both chose a violet one. . . The twins were dressed so alike as to cause greater confusion. Whether it was because of childish malice, or because of a natural law (which the curate maintained they could not escape), as soon as one happened to break his clog's tip, the other soon broke his; if one tore his tunic or cap, the other at once copied the tear so well it seemed to have been caused by the same accident. . . .

"For good or ill their devotion grew with their age and they soon admitted they could not enjoy playing with other boys if one of them was absent. Their father tried to keep one of them with him all day long while the other was with their mother, but this made them both sad, pale and despondent, as if sick. . . ."

Worried about the possible consequences which their inter-dependence and their habit of constant togetherness might bring in the future, the father tried to pit one against the other. If they both did something wrong, he would box Silvan's ears, while telling Landro, "I will forgive you this time because you are usually more reasonable." But Silvan forgot his smarting ears in his joy at seeing his twin spared, while Landro cried as if his ears had been boxed.

Again, attempts were made to give to only one of them something both wanted. But they immediately split it if it was something to eat or shared its use if it was a toy, or passed it back and forth to each other with no distinction between "yours" and "mine." If one was complimented and the other ignored, the second twin was happy and proud on having his brother encouraged and applauded him himself.

Tragedy is precipitated by love. Landro had always disliked and feared little Fadette, considered the homeliest girl in town and suspected of witchcraft. Yet, through a series of incidents, Landro fell passionately in love with her, to the point where he could not think of living without her. She, in turn, loved him with equal ardor, though she did not show it. Landro's parents objected violently to his choice, as did Silvan. Jealous and deeply hurt on finding himself playing second fiddle, he fell ill. Landro and Fadette had to make many sacrifices, including a temporary separation, before they could overcome all this opposition. With kindness and common sense, Fadette succeeded in curing Silvan, who learned to know and love her himself. Since she belonged to his brother, the only solution was for Silvan to leave home and take up a military career, which he did.

Alexandre Dumas used the theme of identical twins in two of his stories, *Les Frères corses* (*The Corsican Brothers*) and *Le Vicomte de Bragelonne* (*The Man in the Iron Mask*).

Mark Twain, the American humorist, in a brilliant dialogue between a twin and a journalist, discusses the troubles that may ensue when two newborn twins are interchanged.

Among works dealing with twins from a psychological viewpoint is the Italian novel *I fantasmi della mia vita* by Achille Geremicca. This is a first-person account of the life of a man with a morbid imagination, unhappy primarily because he is incapable of directing the course of his life. The poor fellow lives in a world of dreams and illusions. He is weak and delicate, feminine in temperament and extremely sensitive. Weary of life, he contemplates committing suicide, but decides he is not only unwanted by his fellows but by the dead as well.

Even in childhood his heart longed for the companionship of a brother his own age who could comfort and strengthen him. For years he waited for this twin soul to find him. Inspired by a legend, he gave his imaginary twin the name of Amile, calling himself Amis. He felt he could never grow to manhood unless he found Amile, whom he imagined to be the image of himself in build and habits. "I, who was naturally timid, peaceable and weak, dreamt of war and fighting, but only if Amile could be at my side."

One day, while still a little boy, he was out walking with the maid, Rosaria, when they chanced to meet an old woman who asked about the lad's health. "He is well," replied the servant, "but very delicate, for he came into the world with another. You know that twins are never very strong."

Regarding this incident Amis wrote, "And so, all of a sudden, and in the street, my heart received a great shock from which it did not recover for many years. . . . Amile was no longer someone to be with in the future, no longer a desire, a hope, but a sorrow and a bereavement. My mind held no memory of my lost companion, but my heart did. . . . Now I knew why I was weak and timid and overcome by my enemies even before fighting them. From the day of my birth I was but a poor survivor, a remaining soul, a mutilated life, a mere half which, by itself, is as sad as a ruin. Twins are made in such a way that two make a perfect creature. The one who survives the death of his brother is a yearning heart that cannot be healed, because it can never be joined to another." Eventually, however, this feeling of emptiness is dispersed when Amis meets and falls deeply in love with a girl who is everything he desires.

With the pen of a fine artist and with deep psychological insight, Wilhelm von Scholz, noted for his dramatic works, poems and philosophical studies, gives a remarkable description of the minds of two twins in a story where mystical happenings and occult forces play a leading role. In Scholz's novel, entitled *Perpetua*, we read of the fate of two sisters, one becoming a saint after having reached an abyss of evil because of passion, and the other dying heroically at the stake in place of her sister who had been condemned for witchcraft.

It seems from birth both these twins had a small red mole shaped like a flame on the right knee. Though Catherine's was redder than her sisters's at first, it later disappeared, leaving only a pale pink outline. Their mother, a superstitious woman, used to worry about these markings. When Catherine was sentenced to be burned at the stake, it was thought this little flame-like mark on her knee had kindled the notion that she was a witch.

At the age of ten the twins resembled each other more than ever. "A surprising likeness in character, thought, will and suffering added to their physical resemblance," wrote von Scholz. "Even those who watched over them carefully, such as their parents, found there were days in which the twins, Mary and Catherine, could be told apart only when they were together . . . The two girls appeared to be as one. And when one of them went out and the other came in, the second immediately took up the game where her sister had left off, or began to fret or cry when, unbeknownst to her, her sister had been scolded or punished."

Yet even at that age there were certain dissimilarities between them as there were in later life. Mary was influenced by Catherine, who was the leader of the two and who always made the first move whenever a decision was called for. In the choice of a game, for example, "one could notice by a slight shake of her head that the thought had first occurred to Catherine." But at once Mary appeared to have wished the same thing. "Playing with other children, they had to submit to the general choice, but they clung to each other and did not lose themselves in the crowd."

So alike were the girls in appearance that they could be taken for a portrait and its model. "They were identical in every respect, in build, hair, eyes, face, voice, walk. . . ." This physical resemblance was maintained as the years went by. After Catherine had been condemned to die, Mary, who had meanwhile become a nun, came to see her. Face to face with her sister, "she suddenly had the impression she was looking into a mirror and seeing herself—the same, yet different." Only the nun's coif distinguished them.

So it came about that at the last moment Catherine was saved by her sister, the nun, who disguised herself in Catherine's clothes and went to the stake in her place. In this way she was able to realize her subconscious wish for atonement and martyrdom. Catherine collapsed and was brought to the convent dressed as Sister Perpetua. There she fasted and did penance. Later she became a saint herself and worked miracles. To the day of her death she was believed to be her sister, Mary.

Aldous Huxley, a brilliant English-born novelist with a profound knowledge of biology, is the author of a unique work of fiction entitled *Brave New World*. In this book, which has become a classic, machinery and dispassionate intelligence are utilized to an extraordinary degree. Here multitudes of twins are produced *en masse* by an incubation and conditioning center. Men are bred "*in vitro*" by a process which affords a high degree of polyembryony, so that many identical individuals come from a single fertilized egg.

However, producing the greatest possible number of twins is not enough. It is also necessary to control and condition the destiny of these individuals, so that (and this applies to every level of society) their physical and psychological development corresponds to their status, to the surroundings in which they live, and the work they must do in order to be useful to society and happy with their lot, envying no one and desiring nothing more than what they possess.

Thus "an Epsilon embryo must have an Epsilon environment as well as an Epsilon heredity." Such embryos are kept in a subnormal state by a deliberate oxygen shortage—"the lower the caste the shorter the oxygen." The first organ affected is the brain, but in the Epsilon type only a minimum amount of "human" intelligence is required, because its members are destined to function as machines.

Having placed the various groups of embryos in an environment that is suitable for life after "decantation" (in lieu of birth), they are taught to love their surroundings and their social standing. "That is the secret of happiness and virtue; liking what you've got to. All conditioning aims at that—making people like their inescapable social destiny."

Huxley describes a lesson in the conditioning of a group of Delta twins destined to grow up with an instinctive hatred of books and flowers. Their reflexes are permanently conditioned in the "neo-Pavlovian conditioning rooms" by means of harsh sounds and electric shocks. Deltas will thus shrink away from books and botany all their lives.

The basic rule of education involved in conditioning the various social groups is that of sleep-teaching or hypnopaedia. "Wordless conditioning is crude and wholesale; cannot bring home the finer distinctions, cannot inculcate the more complex courses of behaviour. For that there must be words, but words without reason. In brief, hypnopaedia. The greatest moralising and socialising force of all time."

These hypnopaedic lessons will be repeated "till at last the child's mind *is* these suggestions and the sum of these suggestions *is* the child's mind. And not the child's mind only. The adult's mind too—all his life long. The mind that judges and desires and decides—made up of these suggestions. But all these suggestions are . . . suggestions from the State."

These stereotyped individuals are the social foundation in Huxley's *Brave New World*. They guarantee a complete though unnatural stability, which is the absolute requisite for happiness. These unnatural creatures, deprived of every liberty, conditioned to contentment, and held in bondage by this conditioning, function as robots in a world where vice is law and the opposite of vice is sin.

In Thornton Wilder's *The Bridge of San Luis Rey*, one of the episodes is about a twin named Esteban. The novel is based on the actual collapse of the bridge in Lima, Peru toward the end of the year 1700. Five people who happened to be crossing the bridge at the time perished when it gave way. Wilder recounts the story of the victims, one by one, tracing the path of providence that led each to his untimely death.

Esteban was one of the victims of the disaster. From birth his life had been an adventurous one. To begin with, he and his twin Manuel had been discovered one morning in a basket in front of a convent. The boys were alike as two peas. The twin brothers became public charges but were well liked by everyone.

"Because they had no family," writes Wilder, "because they were twins, and because they were brought up by women, they were silent. There was in them a curious shame in regard to their resemblance. They had to live in a world where it was the subject of a continual commenting and joking. It was never funny to them, and they suffered the eternal pleasantries with stolid patience.

"From the years when they first learned to speak they invented a secret language for themselves, one that was scarcely dependent on the Spanish for its vocabulary, or even for its syntax. They resorted to it only when they were alone, or at great intervals in moments of stress whispered it in the presence of others. . . .

"This language was the symbol of their profound identity with one another. . . . *Love* is inadequate to describe the tacit, almost ashamed oneness of these brothers. What relationship is it in which few words are exchanged, and those only about the details of food, clothing, and occupation; in which the two persons have a curious reluctance even to glance at one another; and in which there is a tacit arrangement not to appear together in the city and to go on the same errand by different streets?

"And yet side by side with this there existed a need of one another so terrible that it produced miracles as naturally as the charged air of a sultry day produces lightning. The brothers were scarcely conscious of it themselves, but telepathy was a common occurrence in their lives, and when one returned home the other was always aware of it while his brother was still several streets away."

One day the two young men became divided by Manuel's love for a woman. Esteban suffered, not from jealousy but because "there was no room in his imagination for a new loyalty, not because his heart was less large than Manuel's but because it was of simpler texture." Manuel never succeeded in understanding this truth to the full. But he realized that Esteban suffered. Out of this deep affection he tried in every way to keep his brother near him but Esteban only became more distant. And suddenly, of his own free will, Manuel tore the woman he loved from his heart.

So strong was this link between the twins that it triumphed over love, but it could not triumph over death. Manuel fell ill and died shortly thereafter. Wilder gives a striking description of Esteban's reaction to this loss. "Thereafter Esteban refused to come near the building. He would start off upon long walks, but presently drifting back, would hang about, staring at passers-by, within two streets of where his brother lay."

Esteban fell into an extremely disturbed psychological state. He called himself by the name of Manuel and no one was any the wiser for the deception. He wandered around in lonely places. "From time to time he would find work to do, he would become a shepherd or a carter, but after a few months he would disappear. . . ."

One day he tried to hang himself, but was saved by a friend. Whereupon he fell on his face, crying, "I am alone, alone, alone!" A few days later Esteban walked over the bridge of San Luis Rey and was killed in the disaster. In this instance, providence had taken away the life of a poor soul whose brother's death had deprived him of any real reason for living.

In her historical novel, *Gone With the Wind*, Margaret Mitchell gives a vivid description of a pair of identical twins. "Nineteen years old," she writes, "six feet, two inches tall, long of bone and hard of muscle, with sunburned faces and deep auburn hair, their eyes merry and arrogant, their bodies clothed in identical blue coats and mustard colored breeches, they were as much alike as two balls of cotton."

They both loved horseback riding, hunting, dancing and shooting. "They were equally outstanding in their notorious inability to learn anything contained between the covers of books." Romantic episodes in the life of the twins reveal the bond between them. "Until the previous summer," writes Mitchell, "Stuart had courted India Wilkes with the approbation of both families and the entire country . . . . And Stuart might have made the match, but Brent had not been satisfied. Brent liked India but he thought her mighty plain and tame, and he simply could not fall in love with her himself to keep Stuart company. That was the first time the twins' interests had ever diverged, and Brent was resentful of his brother's attentions to a girl who seemed to him not at all remarkable. . . ."

Stuart's marriage plans went up in smoke when both brothers fell in love with Scarlett O'Hara. "Just what the loser would do, should Scarlett accept either of them, the twins did not ask. They would cross that bridge when they came to it. For the present they were quite satisfied to be in accord again about one girl, for they had no jealousies between them."

Stuart and Brent went to war and both were wounded. Later they were both killed in the same battle. "Between the graves of Brent and Stuart there was a stone on which was engraved 'They were sympathetic and affectionate in life, and death has not parted them.' "

4. CONCLUSION

Art and science represent two activities of the human mind which are apparently so clearly separated that they may be called antipodes. They are distinguished by a very different method, the first being essentially guided by a thinking subject, and the second by a thought object. Art is inspired and may take the greatest liberties, while science charts the way, cleaving to the calculated limitations of experimental boundaries. The first is the principal fruit of representation, and the second of ideation; the first a vibrating echo of our emotional life, and the second the dispassionate consequences of our thinking existence.

Though so different and distinct in their end results, art and science have more than one common root and several intertwining branches. Among other similarities, art and science have in common the fact that they are both directed at the search for knowledge. However, the paths leading to this goal are very different in each case, since art is based on intuition and science on reason.

The knowledge that characterizes art is a means of identifying an undeniable reality which might not be reached so easily by abstract thought. An aesthetic pleasure, for instance, allows us to discover and to "know" the beauty of a work of art in a very short time. A rational analysis takes longer, and even then the true meaning is often grasped only with some help from art.

The beauty or plainness of the human body, for example, is sometimes understood more quickly and perhaps better through a sense of intuition than by all the laws of anatomy. Hence, for a thorough knowledge in certain studies, we would do well to have access to both these avenues of expression of the human mind—intuition as well as reason.

In discussing what myth and art have had to say about twins, we cannot help speculating how far art has been able to keep up with science. It should be noted that a distinction has been made in our survey. We have separated the purely artistic creations from those literary works representing an artistic coating around a core of fact established by science. In such instances, art is of secondary importance and we are dealing with artistic sensibility rather than artistic intuition.

Aldous Huxley's *Brave New World* would seem to belong in this category, the author having probably gleaned the detailed scientific background for his book from his uncle, Sir Thomas Huxley, the eminent English biologist. The novel may be classified as another of those quasi-scientific works at which Jules Verne excelled. Yet it seems to us none of them can be regarded as a strictly artistic creation by an author fully inspired by artistry.

To rate the stamp of artistic intuition, a work of art need not shun the true models that life itself makes available to the artist. On the contrary, this is what distinguishes art—to look deep into reality with the penetration of intuition, rather than with the help of whatever technical knowledge the scientist offers. Both artist and scientist start from reality, their paths diverging in the way they regard it, in the particular attitude of their minds, and in the different nature of the work they produce.

On the basis of this distinction, we may divide works dealing with twins into two main groups: (1) those clearly predicated on an interpretation of reality, even though artistic; and (2) those scarcely concerned with reality, except to acknowledge that a human female sometimes produces two beings at a time instead of one. This detachment from reality is particularly manifest in those mythological creations which are reflected in art and in numerous comedies written during the Renaissance and since, which deal with twins of opposite sex who are otherwise absolutely alike in physical as well as psychological attributes.

This kind of art we would term "disembodied." It lacks a model. It is a product of pure fantasy. Since dizygotic twins, such as twins of opposite sex, are genetically unlike, it is highly fallacious to substitute one for the other or endow them with identical qualities, even in a work of fiction.

By contrast, many a literary product clearly bespeaks its objective origin, thereby deserving the label of quality. One of the highest and noblest functions of art is to uncover new perspectives in reality and relate them to the artistic laws inherent in the human mind. This kind of art is best suited for a transfiguration of reality. By presenting a refreshing commentary on human life, it is better able to influence mankind. The best of such works dealing with twins are generally woven around identical pairs. We have seen how art may achieve a glorification of biological truths, such as living twins, and how, when confronted with so mysterious and fascinating a phenomenon as twinning, art may, in its own way, keep abreast or even ahead of science.

Chapter II

HISTORY AND SCIENCE OF TWINS

1. TWINS IN HISTORY

THE REPRESENTATION of twins in art has been based on the existing reality of twins in history. Naturally, the majority of authentic twin pairs, like the majority of men in general, have not been recorded. However, the lives and works of a few of the earliest known twins have come down to us from the distant past.

The first of these famous pairs, Jacob and Esau, are found in the Bible, where we read: "And Isaac entreated the LORD for his wife because she was barren: and the LORD was entreated of him, and Rebekah his wife conceived. And the children struggled together within her; and she said, If it be so why am I thus? . . . And when her days to be delivered were fulfilled, behold, there were twins in her womb.

"And the first came out red, all over like an hairy garment; and they called his name Esau. And after that came his brother out, and his hand took hold of Esau's heel; and his name was called Jacob; and Isaac was threescore years old when she bare them. And the boys grew: and Esau was a cunning hunter, a man of the field; and Jacob was a plain man, dwelling in tents. And Isaac loved Esau, because he did eat of his venison: but Rebekah loved Jacob" (Gen. XXV, 21-28).

The description of these twins clearly indicates they were not identical. Later this evidence is supported when Jacob points out to his mother the difference in his brother's growth of hair, saying, "Behold, Esau my brother is a hairy man, and I am a smooth man" (Gen. XXVII, 11). Rebekah made use of this difference in the famous episode where Isaac, having been deceived, gave his paternal blessing to Jacob instead of his first-born. She got the idea of covering Jacob's hands and neck with goat skins, so that Isaac, who was blind, believed he was touching Esau and bestowed on Jacob the blessing intended to confer special rights on the first-born. However, though Isaac was deceived, he did notice something amiss and remarked, "The voice is Jacob's voice but the hands are the hands of Esau" (Gen. XXVII, 22). Apparently the tone of voice of the two brothers was also different.

Further on in *Genesis* we read of Tamar who gave birth to twins, the father of whom was Judah: "And it came to pass in the time of her travail, that, behold, twins were in her womb. And it came to pass, when she travailed, that the one put out his hand: and the midwife took and bound upon his hand a scarlet thread, saying, This came out first. And it came to pass, as he drew back his hand, that, behold, his brother came out: and she said, How hast thou broken forth? this breach be upon thee: therefore his name was called Pharez. And afterward came out his brother, that had the scarlet thread upon his hand: and his name was called Zarah" (Gen. XXXVIII, 27-30).

We read nothing further of Zarah, but Pharez is mentioned by Saint Matthew (1,3) as an ancient forefather of Our Lord, Jesus

Christ. In the *New Testament* mention is made of another twin, Thomas *didymos* (Greek for twin); the co-twin of Thomas, the Apostle, is unknown.

From classic times, a passage written by Aulus Gellius refers to two births of quintuplets: "Aristotle," he writes, "reports that an Egyptian woman gave birth to five sons at the same time, that this number was never exceeded, and that the case was extremely rare. But also when Emperor Augustus ruled, as I have learned from the writings of the historians of that time, one of Augustus' maid-servants in the Laurentine territory (not far from Rome) gave birth to five babies who survived only for a few days. Their mother, too, died soon afterwards, and by order of Augustus a monument was erected to her on the Laurentine Way, and on it was inscribed the number of children she had borne" (*Noctium Atticarum* X, 11).

In the family of the Caesars, Germanicus' sister, Livia, the wife of Tiberius' son Drusus, gave birth to male twins whose arrival brought much happiness to the imperial household (*Tacitus, Annales* II, 84). Faustina, the wife of Marcus Aurelius (A.D. 121-180) who belonged to the imperial dynasty of the Antonini, gave birth to twins, one of whom later became emperor and assumed the name of Commodus. His twin brother was called Antonius Geminus to distinguish him from his grandfather Antoninus the Pious. The Museum of Naples possesses several medals commemorating Faustina's twin children (Fig. 1).

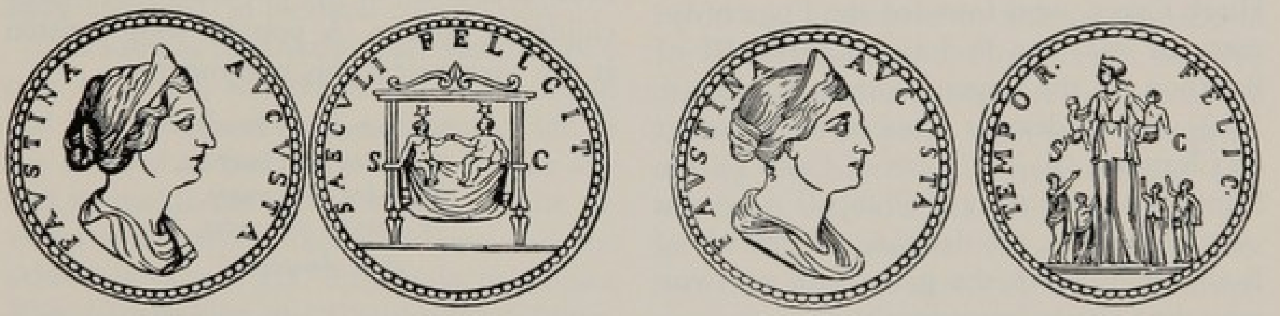


Fig. 1. Medals in honor of Faustina Augusta for her twin delivery of Commodus and Antonius Gemini; on the reverse side of the first medal the twins are in the "cubiculum"; on that of the second medal are Faustina's six sons; the twins are in the arms of Giunone Lucina, the patron of fecundity (Museum of Naples).

Shortly after the fall of the Roman Empire, we find a famous pair of twins, both of whom were saints. They are Saint Benedict, the founder of the first great western religious order, and Saint Scholastica (480-547). The British monk, "the Venerable Bede," mentioned them in one of his sermons in the Eighth Century. The epitaph on the tombstone of these two saints in the Abbey of Montecassino refers to their twin birth:

BENEDICTUM ET SCHOLASTICAM
UNO IN TERRIS PARTU EDITOS
UNA IN DEUM PIETATE COELO REDDITOS
UNUS HIC EXCIPIT TUMULUS
MORTALIS DEPOSITI PRO AETERNITATE CUSTOS

(*Abbot Angelo della Noce*)

In some noble and dynastic families of the Middle Ages and into more modern times, the frequency of twin births as traced on the family tree is very striking. Not only is the phenomenon interesting from a historical point of view but from a biological one as well, for it reveals the hereditary element in twin births, reinforced in these genealogical findings by the frequent inbreeding.

Looking through Ferri-Mancini's *Manuale di Genealogia per la storia del Medio Evo e moderna* (Osimo, 1883), in the tables dealing with the Capetings (descendants of Hugh Capet, who founded the French dynasty in 987) we find that Charles III of Bourbon, of the Capet-Bourbon family (d. 1527)—whose descent is traced from Robert de Clermont (d. 1317) son of Louis IX the Saint, son in his turn of Philip II Augustus —married Susan, the daughter of Peter II of Bourbon. In 1518 she gave birth to twins who died almost immediately.

Among the Condé Princes of the Capet-Bourbon family, we find Louis I (d. 1569). In 1562 he became the father of twin boys, Louis and Charles, one of whom died a year later and the other in 1594. Their brother, Henry I, was the father of Henry II (1588-1646) who in turn was the father of twin sons born in November 1618, and dying that very month.

The royal family of the Bourbons derived from this branch of the Capet-Bourbon Princes. It is interesting to note that the occurrence of twins continued. Louis Philip II Égalité (1747-1793) son of Philip I, was father to twin girls born in 1777. One of them died almost at once, and the survivor became known as Adelaide d'Orléans. In the same family we find Louis XV, the third nephew of Louis XIV the Great (d. 1715), who was related to the kings of Sardinia on his mother's side.

Louis XV (1710-1774) married Mary Leszczynska (1703-1768) and they had twins, Louisa Elizabeth and Henrietta Anne, born in 1727. Cabanès (in *Moeurs intimes du passé*, Paris, Michel 1923) mentions the now well-known remark made by the obstetrician at the birth of these twins. Having delivered the first girl and knowing a twin was to follow, he was hoping the second child of the primiparous queen would be a male heir. On seeing the second baby girl he exclaimed in a melancholy voice, "*Cela ne vaut pas un dauphin.*" When the people heard about this twin birth, they became alarmed at the potential cost of the children's upkeep. A popular song written at the time voices this sentiment:

> "*Il faudra deux bonnets*
> *il faudra deux hochets,*
> *il faudra deux maris,*
> *et l'année qui vient,*
> *deux dauphins.*"

The twins were called "Madame Première" and "Madame Seconde." Louis XV was very proud of this birth and ordered a medal to be struck in honor of it. Louisa Elizabeth later married Philip, Duke of Parma. Henrietta Anne, who suffered (as did her sister, though less severely) from a skin disease, probably of allergic origin, remained unmarried.

Philip of Bourbon, uncle of Louis XV, became King of Spain and took the name of Philip V (d. 1746). His nephew, Charles IV (1748-1819) married Louisa, daughter of Philip, Duke of Parma, and had twins—Charles and Philip, who were born in September 1783.

In Germany, in the house of Nassau and royal families deriving from it (Hesse, Holstein-Gottorp, Baden, Bavaria, Brunswick, Lippe) twin births seem to have been quite common. According to some authors, they also occurred rather frequently in the history of the Hapsburgs.

Among the twins of particular historical significance is Saint Catherine of Siena (1347-1380). In the life story of this saint, written by her confessor and biographer Raimondo da Capua, we learn certain facts about Catherine's father and mother, Giacomo and Lapa: "While Lapa . . . through her frequent pregnancies filled Giacomo's house with sons and daughters, towards the end of her child-bearing life she happened to conceive and give birth to twin girls. . . . And so she was delivered of these twins, weak of sex and still weaker, as it immediately appeared, in physical constitution. . . .

"As soon as the mother had seen her two tiny creatures, she realized that she could not suckle both of them sufficiently, and so she decided to find a wet-nurse for the one and to suckle the other herself . . . the favored child was called Catherine and the other Giovanna" (D. Raimondo da Capua, *Vita di Santa Caterina*, Chapter II). Giovanna died almost at once. The author goes on to say that Lapa gave birth to other twins.

More recently, another twin who may soon be sainted is the Peruvian Servant of God, Luisa de la Torre Rojas (1819-1869).

In 1600, in Hameln on the Weser, a Mrs. Römer gave birth in one delivery to seven children who died soon after birth. A famous bas-relief commemorates this most extraordinary event.

The Swiss twins, Augustus and Jean Piccard (the first a physicist and the second a chemical engineer, both very well known), are mentioned later on in this volume, as are the Dionne quintuplets and other famous multiple births of modern times.

In regard to legal questions pertaining to twins, the Jewish law considered the first-born of a pair to be the first heir, while the intermediate law, through the influence of the *ius francorum*, stated that the second-born should be the first heir because it was conceived first. It is worth noting that both the Roman and modern law consider the first-born to be the first heir. However, the order in which twins are born has very little influence on our present-day concept of legal rights, except when dealing with a succession to the throne, or matters concerning the nobility, or disputed wills.

2. HISTORICAL DEVELOPMENT OF THE SCIENTIFIC STUDY OF TWINS

Long before medicine developed into a full-fledged science, doctors, naturalists, and other scholars focused attention on twin births and attempted to find an explanation for this phenomenon. Hippocrates believed twins were conceived by the division of the sperm into two parts, with each part penetrating one of the two uterine horns (*De nat. pueri*, ed. Focs, III, 248). Andreassi observes that in ancient times the twin phenomenon was associated with double formations. Empedocles believed them to be due to an excess of sperm emitted at one time, while Democritus ascribed them to sperm emitted at different times, each time corresponding to an embryo.

Andreassi writes: "Double monstrosities, according to Aristotle, would originate from a phenomenon of co-development whereby two embryos, originally separate, reach a partial fusion, thus making a single formation, whose components, however, are still distinct. In other words, there would be two embryos at first, as in any twin pregnancy, followed by a variable degree of coalescence. . . . Double formations occur more often in animals which are normally multiparous than in normally uniparous ones. This would explain why such double formations are much less frequent in man. . . .

"Aristotle also adds, very cautiously, that while he believes double formations originate by co-development, should the cause be found in the male sperm, Democritus' theory would be more plausible. By expressing this opinion, he indicates that the causes might be multiple. Galen seems to accept Empedocles' hypothesis, adding that excess heat in the uterus might split the sperm, thus originating two or more formations. Plinius adds no new ideas but simply reports multiple births in detail."

It is interesting to note Cicero's comments on what Diogenes had to say about twins and astrologers, who held that the life, soul and disposition of every man was determined by the influence of the stars: "Even Diogenes, the Stoic, admits certain things. For example, that the stars can only predict the temperament a man will have, or what he will best succeed in. He declares that the stars have no power to foretell anything else; and that though the appearance of twins is similar, their lives and living conditions are generally different. Procles and Euristenes, kings of the Spartans, were twins but they did not live for the same number of years. Procles died a year before, though he greatly surpassed his brother in the glory of his feats" (Cicero, *De divinatione*, II).

Fig. 2. Pregnant uterus containing dichorial twins and opened anteriorly, prepared in wax by the sculptor, G. B. Manfredini; the original was provided by the anatomist, Carlo Mondini of Bologna. (Rome, Hospital of Santo Spirito in Sassia, Museum of Medical Art.)

St. Augustine, Bishop of Hippo, in his *De civitate Dei* (Book V, Chapter II and foll.) states: "Cicero says that the famous doctor, Hippocrates, has written about certain brothers who, falling ill together of a disease which became aggravated and then ameliorated at the same time in both of them, were considered by him to be twins. Posidonius, a Stoic philosopher who was passionately dedicated to astrology, declared that these twins were born and conceived when the stars were in the same position. The philosopher-astrologer therefore believed this phenomenon depended on the position the stars assumed when the twins were conceived and born, while the doctor attributed it to the fact that the twins had a very similar temperament."

During the many centuries dominated by the Arabic and Salernitan schools of medicine, writers merely reiterated the ideas about twins already expressed by the old classic authors. During and following the Renaissance the subject was approached indirectly through studies of double monstrosities, and also by direct obstetrical observation. With the invention of printing, many xylographs and metal engravings were made in honor of twin births, especially representing the positions assumed by twins in the uterus (see Chapter VIII).

Medical research workers considered twins essentially from an obstetrical point of view, noting the differences that may occur in the pregnancy and birth of twins as compared with single births. The fine wax representations in the museum of the Hospital of Santo Spirito in Rome, here reproduced for the first time (Figs. 2 and 3), are authentic masterpieces. They show an

Fig. 3. Representation of two monochorionic twin fetuses with a single placenta (prepared in wax, as in Fig. 2).

amazing knowledge of the ovular membranes in twin pregnancy. Among the additions to obstetrical information we find such worthy items as Viardel's report in 1671 that uniovular twins are always of the same sex.

It was not until the second half of the Nineteenth Century that the phenomenon of twinning ceased to be regarded as something of a biological whim which aroused either a sense of alarm or idle curiosity, depending on the circumstances. It was Sir Francis Galton (Fig. 4) who had the foresight to propose the use of twins as a research tool in the service of science.

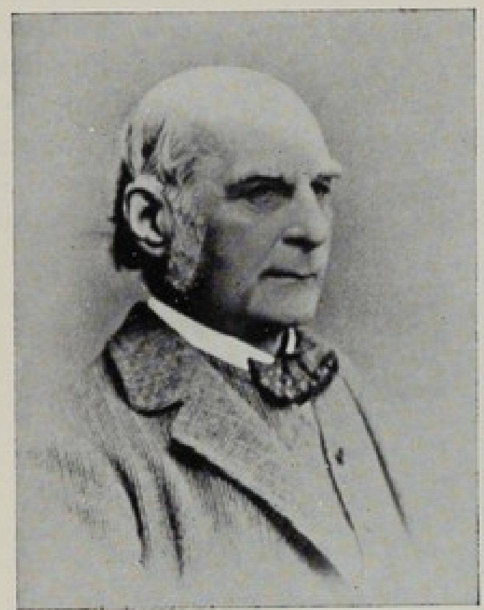


Fig. 4. Sir Francis Galton at the age of 73.

Before Galton, twins were in a class by themselves in the eyes of medical authorities. It was accepted that they came from a multiple pregnancy which was characterized by specific symptoms, required a special technique, and led to the birth of individuals who needed special attention and care to offset the danger in which they lived. Twins held an interest all their own; they were the start and the finish of a scientific argument.

During Galton's time and since then, twins became the instrument for scientific procedures whereby many medical objectives could be gained. The innumerable research programs being carried out on the subject of twins in all parts of the world, and the valuable contributions they are making to the progress of medicine demonstrate that the new road opened up by Galton was well illuminated and destined to lead to the peaks of knowledge. Following is a brief review of the development of twin studies in various countries.

Austria and Hungary

The geminological schools of Austria and Hungary have been very productive. Spaeth, a Viennese obstetrician, was one of the first workers, as far back as 1870, to make a clear distinction between uniovular and biovular twins. His studies were continued by Julius Bauer, who stressed the value of twin studies in his *Vorlesungen über allgemeine Konstitutions-und Vererbungslehre* (1921).

Other noted members of the School of Vienna were the pediatrician Stransky, whose observations on some 200 pairs were published in 1937; Bouterwek, who reported on 120 pairs; Geyer, Hartmann, and Stumpfl.

In Budapest, interesting twin studies were conducted by Adele von Jankovich-Simon (141 pairs at the Pàzmàny Péter Institute of Hygiene), Román-Goldzieher (handwriting in 283 pairs), Szendi, and others.

Benelux Countries

In Holland, H. W. Siemens of Leiden deserves credit for opening a new approach to twin studies. In his book on the pathology of 52 MZ pairs and 36 DZ pairs, he made two contributions. First, he laid the foundation for the use of the similarity method, based on comparison of intrinsic twin characteristics rather than fetal-membrane reports. This method was later improved by von Verschuer. Also, Siemens used twin studies for purposes of clinical investigation rather than for purely statistical reasons, and emphasized the need for the use of unselected (representative) twin samples. Similar ideas were later expressed by Luxenburger and Weitz in Germany, and by Kallmann in the United States. In the words of Luxenburger, Siemens' book possesses "an historical character."

Other Dutch workers of note were P. J. Waardenburg, who was interested especially in the neurologic and ophthalmologic aspects of twin studies (and himself became the father of two female MZ twins); the late Legras, who studied criminality in twins and Polman, author of *Een-en Tweeëiige Tweelingen;* Schokking, Versluys, and Voûte.

Belgian twin researchers included Dalq (noted for embryological studies of twins), Aubel, François, Ley, van Bogaert, and Verhal.

East European and Balkan States

Among the East European countries, the Soviet Union has shown the greatest interest in the study of twins. At the Maxím Gorky Medico-Biological Research Institute in Moscow, extensive interdisciplinary twin studies were conducted under the direction of S. G. Levit. Special dormitories were available for the observation of the many research subjects.

Well-known names in this field include those of Bossik, Burrak, Gurevich, Ignatjev, Kabakov, Kanajev, Kasparyan, Kolbanovsky, Mirenova, Passyukoff, and Ryvkin. Special mention has been made elsewhere of Michael Zawadowsky, who did such fine work with twinning in sheep.

Finland is represented by the work of Brander, Klemola, Lehtovara, and Suomalainen; and Czechoslovakia by that of Kadlečik, Lukáš, Matoušek, and Seemann.

In Bulgaria, we have Kadanoff; in Poland, Jablonski and Kisslowsky; in Rumania, Cohl, Ionasiu, Marinescu, and Spirea; and in Yugoslavia, Lopaštic.

England

As previously noted, one of the pioneers in twin research was Sir Francis Galton. A native of Duddeston, Warwickshire, he was born in 1822, the same year as Gregor Mendel. Galton, a cousin of Darwin, was descended from a long line of naturalists. During his extensive travels, Galton divided his time among many diversified subjects, including meteorology, the physiology of the sensory organs, and, of course, genetics and eugenics.

In the field of twin studies, Galton published two books that have since become famous: *The History of Twins as a Criterion of the Relative Powers of Nature and Nurture* (1875), and *Inquiries into Human Faculty and Its Development* (1883). Searching for "a new method by which it would be possible to weigh with a just balance the effects of heredity (nature) and environment (nurture)," he discovered the usefulness of twins. By this means he believed it would be possible to distinguish "between the effects of tendencies received at birth and those imposed by special circumstances in later life." Galton's name lives on in the work of the famous Galton Laboratory of the University College in London.

Other prominent British workers in the field have been Burlingham, Eysenck, Sir Ronald Fisher, Haldane, Harris, Herrman and Hogben, Kalmus, Penrose, Fraser Roberts, Slater and Wingfield.

France

Of historical interest are Féré's *La Famille névropathique* (1894), dealing with the psychiatric aspects of twin studies, and Poyer's *Les Problèmes généraux de l'hérédité psychologique* (1921), which contains a chapter on the significance of twins in the psychological sphere. There were two books entitled *Les Jumeaux*, one by Apert in 1923, and the other by Lamy in 1949. In the obstetrical field, a fine contribution was made by Favreau and Beurois.

Turpin deserves mention for having established a clinic for twins and their health problems. The data so accumulated formed the basis for Zazzo's psychometric studies. Of equal importance was Caullery's work on the methodology of twin studies, summarized in the monograph *Biologie des Jumeaux, polyembryonie et gémellité* (1945).

Germany

Although Virchow had already been interested in problems of concordance in uniovular twins, the foundations of the German gemellological school were laid by the dermatoglyphic work of Poll (1914) and the improvement of the modern similarity method by von Verschuer. The latter, like Siemens, recognized the scientific value of studying not only similar twins, but also the previously neglected category of dissimilar pairs. His investigations were carried out first in Berlin-Dahlem at the *Kaiser Wilhelm Institut für Anthropologie, menschliche Erblehre und Eugenik*, the Max Planck Institute, then, from 1936, at the *Institut für Erbbiologie und Rassenhygiene* of the University of Frankfurt-am-Main, and now at the *Institut für Humangenetik* of Münster University.

The Dahlem group included such well-known names as Curtius, Frischeisen-Köhler, Glatzel, Lenz, Steiner and Werner. Their work was organized with the aid of several large Berlin hospitals. Here the system was introduced of noting the presence or absence of twinning status on the face sheets of patients' records, thereby providing valuable data for various research projects.

At Frankfurt, von Verschuer teamed up with Diehl in an important twin study of pulmonary tuberculosis, the findings of which were published in two volumes under the title of *Zwillings-Tuberkulose*. Other collaborators during this period were Kahler and Weber, who studied heart disease in twins; Claussen (rheumatic fever); Kober (cancer); Krüger and Liebenam, who did regional investigations of twin births. During the postwar period, von Verschuer's associates included Duis, Grebe, Koch, Lehmann, and Wendt.

Other German twin research centers were the Medical Clinic of the University of Munich, where studies of twins were conducted by Brandt and Weihe under Schittenhelm; the Pathological Institute of the University of Berlin (Rössle); and the Max Planck Institute of Psychiatry in Munich, which boasted such prominent twin research workers as Hans Luxenburger (schizophrenia), Johannes Lange (criminal behavior), Thums (cerebral palsy), Conrad (epilepsy), Idelberger (congenital malformations), and Juda (mental deficiency).

From Munich, Lange took the twin study method to the University of Breslau, where he was professor of psychiatry and, among other projects, worked with Kranz and Stumpfl on the subject of criminal twins; while Kallmann, meanwhile, brought his own interest in twin studies to New York.

Twin studies were also developed by Weitz at the Stuttgart Institute of Human Genetics and Twin Research with the aid of Camerer, Kaufmann, Ostertag and Scheerer. Among the many journals that published articles on twins was the *Zeitschrift für menschlische Vererbungs-und Konstitutionslehre*. An excellent review of important twin data compiled up to 1937 is contained in Reinhold Lotze's book, *Zwillinge*.

Italy and the Iberian Countries

Although Rome is the city of Romulus and Remus, Italy did not particularly distinguish itself by an interest in twin studies before the 1940's. Apart from a number of earlier statistical investigations, notably those of Patellani (1911), work on twins was done in the obstetrical and developmental areas by Somaglia, Vaccari, Borrino, and Mino; on psychiatric problems by Esposito; and on ear lobe form by Dalla Volta.

Probably the best known earlier monograph on twins was *I Gemelli* (1926) by the noted Italian anatomist Chiarugi, who subsequently made valuable contributions to the embryology of twinning. In Milan, Professor Luisa Gianferrari, as director of the Human Genetics Center, brought the usefulness of twin research to the attention of municipal hospital authorities.

In 1942 the present writer, stimulated by his work on blood glutathione, founded the Roman center for twin studies, which a few years later sponsored the *Società Italiana Gemelli* (1945), as well as a special clinic for twins at the university. The research work of the center was carried on in collaboration with Benigni, Bianchi, Bini, Calderoni, Capelli, Casa, Cherubini, Iannaccone, Lewis, Maltarello, Manna, Miglio, Pignatelli, Rédeky, Sacco, and Torrioli.

As a special service to the twins themselves, the center opened a summer camp for twins at Manziana (Figs. 5 and 6), with the financial support of the Pontifical Commission for Assistance. In addition, several entertainment occasions for Roman twins were organized, and the *Società Italiana Gemelli* collaborated in the production of a documentary film, "*Fantasia di Gemelli*," under the direction of Marcello Baldi (Fig. 7).

In 1953 the Gregor Mendel Institute for Medical Genetics and Twin Research was opened in Rome by the writer. The clinic facilities developed there helped promote mutual feelings of understanding between doctors and twins—an important prerequisite for successful twin observations. Added impetus in this field was derived from the publication of the first edition of this book, *Studio dei Gemelli* (1951), and that of a journal specializing in twin data, *Acta Geneticæ Medicæ et Gemellologiæ* (1952).

In the Iberian countries, twin research has also had active support. The list of Spanish investigators includes Ayres de Azevedo, Boero, Eschevaria, Hernandez, Horo-Garcia, Martinez, Sanchis, and Villaverde. In Portugal, the work of Bastas and Pacheco and their associates may be mentioned.

Japan

Apart from the studies of Wagenseil in China, and Duncan and Maynard in Australia, the Western Pacific area is represented primarily by Japan as a producer of twin data.

The main topics of interest have been the anatomic, anthropologic and hematologic problems of twins. These studies have been connected with an impressive array of names, including Araki, Cho, Fukuoka, Higeta, Katsne, Kikuchi, Kishi, Koya, Komai, Komatu, Kuragami, Kurita, Mochizuki, Mogi, Morikawa, Morita, Obanai, Oguchi, Oku, Tanaka, Taniguchi and Tsuchiya.

North America

In Canada and the United States, twin research benefited greatly from the early development of clinical and experimental genetics as scientific disciplines, and, in turn, contributed in many ways to the progress of the medical, biological and behavioral sciences.

In the area of normal personality variations, early pilot studies were those by

Figs. 5 and 6. Life of the Italian Society of Twins. 5 (*Upper*). A meeting of twins from Rome. 6 (*Lower*). The male section of the Colony for twins in Manziana.

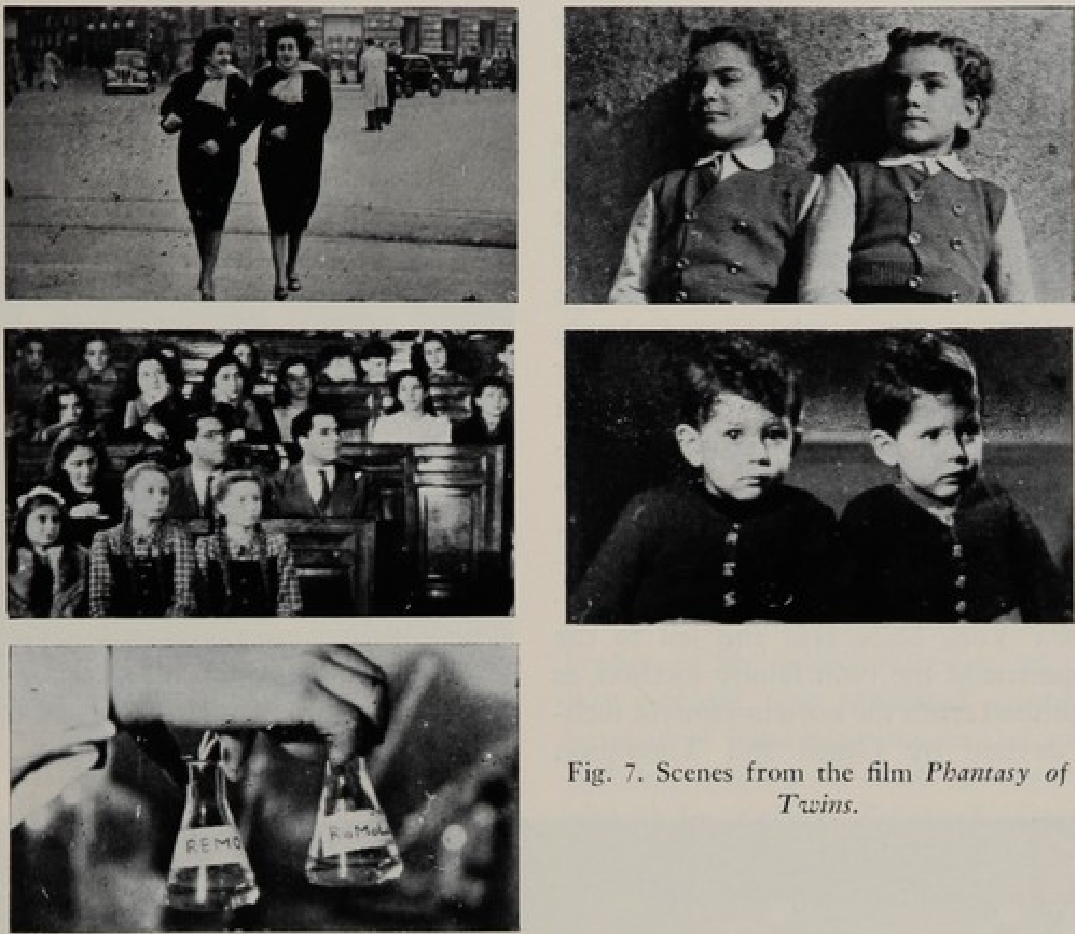


Fig. 7. Scenes from the film *Phantasy of Twins.*

Thorndike (1905), Rosanoff and Orr (1911), Newman (*The Biology of Twins*, 1917 and *The Physiology of Twinning*, 1923), and Gesell (1922). They were followed by the fine work of Cummins, Danforth, Dorn, Lauterbach, Merriman, Muller, and Rife's group at Ohio State University.

Other meritorious contributors were Norma Ford Walker of the University of Toronto, Fraser, Frumkin and others in Canada, where the Dionne quintuplets aroused enormous interest for many years, and such well-known investigators as Gardner, Gowen, Greulich, Keeler, Mayer, Schwesinger, Snyder, Stiles, Warner and Wiener in the United States.

Special mention may be made of the human genetics centers at Chicago University (Strandskov, Thurstone, Wright), Columbia University (Dunn, Gartler, Kallmann, H. Levene, Ph. Levine, Osborn, Shapiro), and Michigan State University (Cotterman, Neel, Sutton, Vandenberg); also, the interesting studies conducted by Burks as well as by Newman, Freeman and Holzinger on identical twins separated in early childhood. *Twins, a Study of Heredity and Environment* (1937) by the Chicago team received widespread attention, as did the experimental work on spontaneous twinning in the armadillo carried on by Newman and Patterson.

In the specialized fields of medical and psychiatric genetics, twin data of more than historical interest were collected by Glass (physiology), Herndon and Jennings (poliomyelitis), Jervis (mental deficiency), the Lennox group in Boston (convulsive disease), Rosanoff and his associates (delinquency, infectious diseases), and Kallmann's twin research team organized at the New York State Psychiatric Institute in 1936.

The twin population studies of Kallmann's group were focused on the endogenous psychoses, mental deficiency, suicide, male homosexuality, aging and longevity, deafness, and pulmonary tuberculosis, and were summarized in his widely read book, *Heredity in Health and Mental Disorder* (1953). Among his collaborators have been such well-known names as those of Gordon Allen, Anastasio, Aschner, Baroff, Falek, Feingold-Jarvik, Planansky, Rainer, Reisner, Roth, Sander, and Sank. The investigations of this group covered the entire New York State area and led to the development of the twin family method, as distinguished from the cotwin-control technique devised by Gesell and Thompson (1941).

Before any other country, the United States has promoted twin research by establishing social organizations for twins and other multiples. Wiggam and others reported on a "Twin Matinée" held at the George M. Cohan Theater in New York City (1921) and a meeting in Mecklenberg County (1930). In 1931, the National Twins Association was founded, and somewhat later a National Association for Triplets. Well-attended meetings were held at Fort Wayne (1937), Chicago (1938), Waterville (1938), New York City (1939) and Baylor University (1941), and the consequent publicity was effectively used by a cosmetic company to advertise its products. Photographs of attractive twins and triplets who attended some of these meetings are reproduced in Figures 8 and 9.

Fig. 8. Triplets who took part in a meeting of the American Association of Triplets held at Palisades Amusement Park.

Fig. 9. Hollywood Twins.

Most of the scientific reports of the North American schools of twin researchers have been published in the *Journal of Heredity*, the *American Journal of Human Genetics*, the *American Journal of Psychiatry*, and the *Eugenics Quarterly*.

Scandinavian Countries

In the country of Linnaeus, work on twins covered the entire range from plants (Muntzing), through the animal studies of the Bonnier school, to humans. One of the leaders in human gemellology was Gunnar Dahlberg, Director of the Human Genetics Institute at the University of Uppsala. Among his early works is *Twin Births and Twins from a Hereditary Point of View* (1926), a book that has since become a classic. Up to his untimely death in 1956, he promoted interest in twin research in many ways, not the least of which was to found the Journal *Acta Genetica et Statistica Medica*, published by Karger.

Other Swedish twin researchers have been Böök (Dahlberg's successor at Uppsala), Borgström, Brattström, Eredström, Josephson, Larson, Lundström (dental aspects), Norinder (handwriting), Romanus, and Sjögren (neuropsychiatry). A major part of the Swedish literature on twins may be found in the journal *Hereditas*.

In Norway, twin studies of various kinds have been conducted by Kristine Bonnevie, Haeggström, Looft, Mohr, Söderström, Sverdrup, and Wedervang.

The Danish school has been under the competent leadership of Professor Tage Kemp of the Institute of Human Genetics of the University of Copenhagen. In celebration of his sixtieth birthday, an anniversary volume was published containing a number of important reports on twins. In addition, much good work has been accomplished by Bartels, Eskelund, Granström, Guldberg, Harvald, Hauge, Heinoneni, Helweg-Larsen, Krabbe, Levison, and Wigers.

South and Central America

Valuable contributions to our knowledge of twinning have also been made by workers in the Latin-American countries. Specifically, we note the names of Deluca, Fernandez, Malbran, Monteiro, Notti, and Widakowich in Argentina; Bittencourt, Dutrey, Locchi, and Vaccarezza in Brazil; Consino and Schwarzenbergh in Chile; Peluffo in Uruguay.

In Mexico, twin research was conducted by Mateos-Fournier, Mena-Brito and Salas-Martinez.

Switzerland

Swiss contributions to twin research, ably supported by the editorial policies of the *Archiv der Julius Klaus-Stiftung* and the *Journal de Génétique Humaine*, have been both substantial and diversified.

In the Zurich group, we find such well-known names as those of Buschke, who began his radiological twin studies at the Zurich Radiology Institute before going to Washington; the ophthalmologists Huber and Vogt who, in collaboration with Wagner, Richner and Meyer, made excellent and well-documented studies on aging twins; Eugster, whose monograph on thyroid conditions was based on a series of 520 pairs of twins; also, Hanhart, Pfändler, and Martha Kuensch (tuberculosis in twins). Other outstanding workers were Berheim-Karrer, Pfister, Bamatter, Linder, Luchsinger, Lüscher, Strupler, and Schlagninhaufen.

At Geneva, a very active group at the Ophthalmological Institute has been headed by Franceschetti and Klein.

Chapter III

TWINS IN PLANT AND ANIMAL LIFE

1. TWINS IN PLANT LIFE

Scientists concerned with plant biology began studying twin organisms before those dealing with animal biology. While observations made by research workers in plant life are rather scarce and fragmentary up to the present time, they need to be recorded. The existence of twin growth in plants has been definitely established, chiefly among spermatophytes (plants with seeds). For example, when seeds of the *Datura stramonium* are sown, a greater number of plants is obtained than the number of seeds used. It is therefore logical to suppose that some of the seeds have produced two or more organisms which may be regarded as twins (Satina, Blakeslee and Avery, 1935).

Seeds producing two or more plant organisms apparently contain two or more embryos, but their genesis has not yet been satisfactorily explained. Botanists are inclined to believe in the existence of different processes of twinning. First, it is possible that from a single fertilized oösphere two embryos may be produced by a process similar to that attributed to monozygotic animal twins, as has been verified by means of cytological observations.

Secondly, twins may originate not only from the occurrence in the ovum of a single fertile macrospore (embryonic sac) but also of two or more fertile macrospores which may later produce the same number of female gametophytes, each containing one oösphere. Following fertilization, each will produce its respective embryo. The way in which more fertile macrospores come together in these ova is not clear. However, there may be a variant factor in the tetragenesis, which normally leads to the formation of four macrospores, three of which are destroyed, while only the fourth is conserved and forms the embryonic sac. In certain cases not only one but two or more of these macrospores may undergo the transformation into embryonic sacs.

Regardless of how they are actuated, it is certain that the embryos present in the same seed, and deriving from the same number of embryonic sacs, have the same biological significance as animal twins produced by different egg cells, and like them, contain a heritage that is only somewhat similar but not identical.

Moreover, since the oösphere becomes divided before fecundation, one half may be fertilized in the usual manner, giving rise to a normal embryo, while the other half may develop parthenogenetically, producing an haploid structure (Pope). Seeds containing two or more embryos are called "twin seeds."

Satina, Blakeslee and Avery (1935) discovered in a seed of *Datura stramonium*, produced by a hybrid plant, two twin embryos of different color. This showed (1) that Mendel's law of the segregation of characters occurs in the same twin seed, and (2) that the zygotes or respective gametes from which such embryos are derived would be separate and different.

Thus in modern plant biology one is inclined to acknowledge the existence of mono- and multizygotic twins. It is necessary to induce the development of twin plants to establish the similarity between all the hereditary characters (monozygotic plant twins), or the differences between them (multizygotic plant twins). Patterson (1919) discovered that mango seeds (seeds of the *Eugenia jambos*), and those of certain fruits sometimes contain more than one embryo. During the course of research (1919) on the alfalfa (*Medicago sativa*), Southworth noticed two young plants produced from a single hybrid seed (Fig. 10). Other times this was not possible because of adhesions which made one of the two plants grow parasitically on its twin.

Waller (1934) described the presence of Siamese twins in the iris (*Chaemaerisis*). As may be seen in the photograph in Figure 11, the plants are intimately united and, according to the author, come from the same seed. Waller observed that only when the plant is in flower, it will be possible to decide whether the twins are "identical" or "fraternal."

Yamamoto (1936) noted on several occasions the presence of a triploid partner in the seed of two Japanese and one Manchurian variety of the *Triticum vulgare*. In the Schinchunaga variety, out of 8,800 seeds the author found 18 twin pairs, three of which were triploid-triploid and all the others only diploid. On one occasion, he found a seed carrier of a triplet triploid-triploid-diploid structure. While the individual organs of the triploid plants were evidently larger than the same organs in diploid plants, the comparative size of the

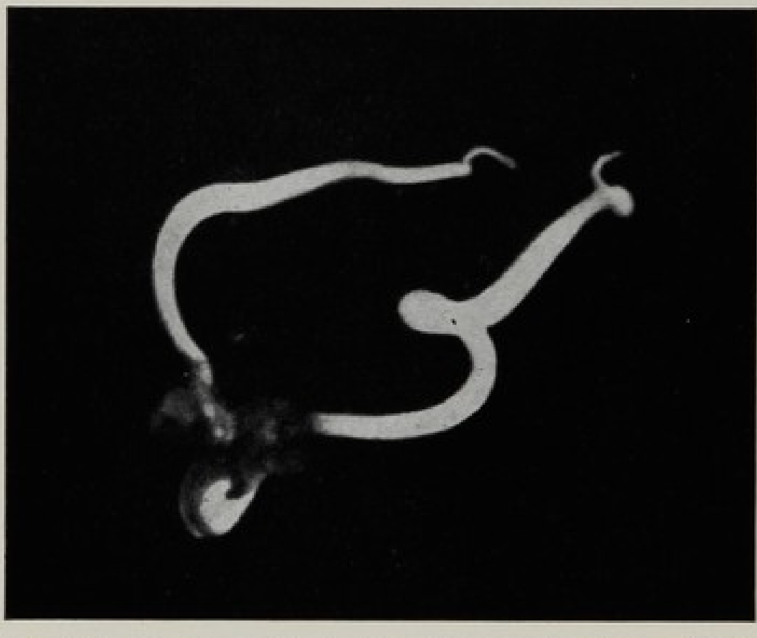


Fig. 10. Two young plants of *medicago sativa* from a single seed (Southworth).

In 1928, Owen studied the heredity of color in the soya and observed that some of its seeds contained two embryos. Out of 5,000 seeds he found 22 cases or 0.44% of diembryony. The author acknowledged the existence of a monozygotic and a dizygotic diembryony. In the latter, there is one pericarp, but the seeds show an independent segregation in regard to the color of the cotylaedons. When diembryonic seeds were sown, it was sometimes possible to separate the young twin plants from each other.

Fig. 11. Siamese twins of the iris (Waller).

Fig. 12. Twins of the linseed; the small roots originate from two embryos contained in the seed (Kappert).

Fig. 13. Incompletely separated twin linseeds (Kappert).

whole plant did not seem to follow any particular rule. The triploid plants produced by autofecundation gave 21% of normal plants, and, by fecundation with normal pollen, 69%. The pollen of triploid plants, when used to fertilize the diploids, gave no result.

Kappert (1933) conducted exhaustive studies on hereditary polyembryony in *Linum usitatissimum* (flax). Producing hybrid flax by crossing carriers of different heredities, he obtained seeds of normal outward appearance which upon germination produced two roots. They developed into two separate plants whose mutual resemblance was greater than in any other case (Fig. 12).

Kappert also demonstrated microscopically that these seeds contained two embryos, obtained by the splitting of a single fertilized oösphere (Fig. 13). Even in flax, he found double malformations consisting of cases of incomplete division of monozygotic twins (Fig. 14). He also observed the

Fig. 14. Twin embryos of the linseed. (Kappert).

development from single linseeds of three or four young plants (triplet and quadruplet plants). These findings convinced the author that twin growth in flax is a hereditary phenomenon and, on the basis of his observations, he came to the conclusion that predisposition to twinning is transmitted through the female plant, although it is the result of a combination of hereditary factors.

Having investigated twin seeds in corn, Horovitz and Sanguineti (1936) came to the conclusion that the formation of such seeds in certain varieties of Argentine corn is a hereditary characteristic. It is interesting to note that the twin plants described by these authors nearly always appear completely or partly united, reminding us of the double monstrosities that occur in animals. The authors suggest that the coalescence of the phenotypes (be it greater or lesser or absent) is an important factor in determining at what time during the development of the embryo the twinning mechanism acts on the seed. In any case, it seems clear that this may happen at various times.

Pope (1943) stated that polyembryony occurs in the barley of Manchuria. Specimens obtained ten and twelve days after artificial pollination showed the presence of two clearly separated embryos in the same seed (Fig. 15).

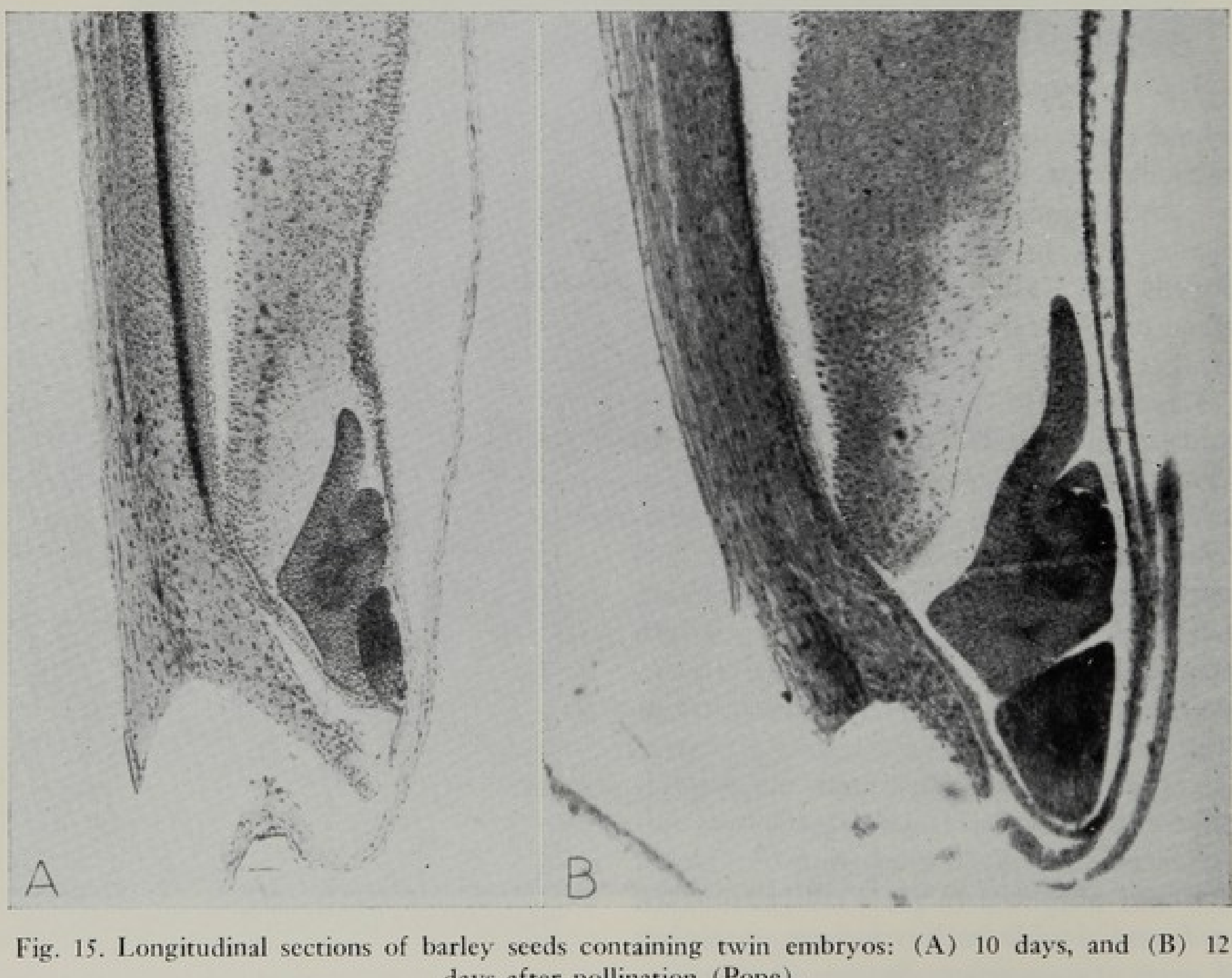


Fig. 15. Longitudinal sections of barley seeds containing twin embryos: (A) 10 days, and (B) 12 days after pollination (Pope).

2. ANIMAL TWINS

The frequent and diversified occurence of the twinning phenomenon in the animal kingdom may be classified under two headings: Artificial and Natural. Artificial twinning is that which is obtained through treatment of the fertilized egg as indicated by the physiology of embryonic development. (Such treatments will be considered when dealing with twin embryogenesis.) Obtaining twin organisms by artificial treatment of single eggs is very important for twin studies. It is assumed that spontaneous twinning may also occur in such eggs. We must distinguish between natural twinning and that induced by artificial means, if only because artificial polyembryony produces individuals whose body size is proportionately reduced, while, in spontaneous animal polyembryony, individuals quickly reach normal size.

One might perhaps suppose that spontaneous twinning may occur in animal species for which spontaneous cases of double monstrosities (incomplete separation of the bodies of monozygotic twins) are reported. However, there are reservations to this supposition because the occurrence of double monstrosities does not always prove that true, complete twinning may be brought to term in a given species.

Natural twinning may be subdivided into habitual and sporadic kinds. The first occurs among physiologically multiparous species, such as swine, rodents, carnivore and the like, with normally multiple births. Sporadic twinning, on the other hand, is that which occurs in rare instances in normally uniparous species, such as equines, bovines and man.

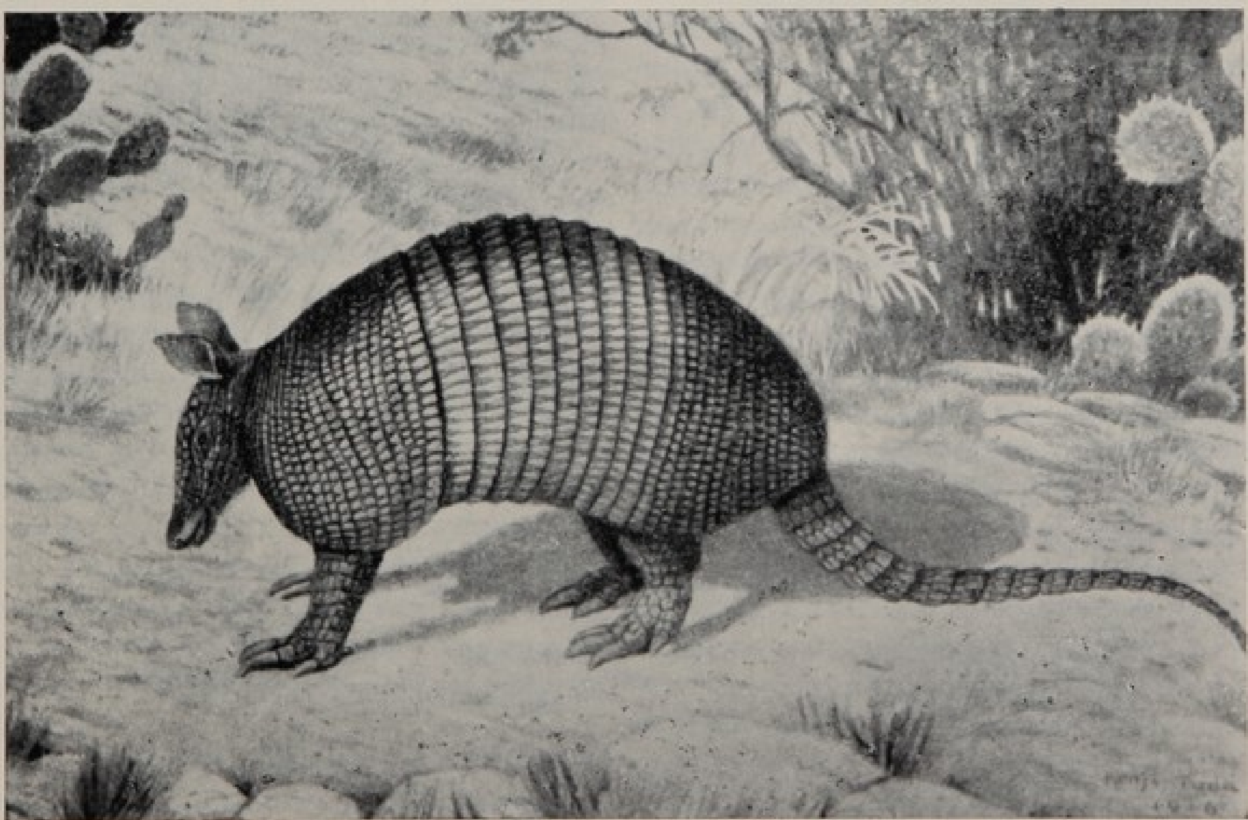


Fig. 16. *Dasypus novemcinctus Texanus* or *Tatusia novemcincta L.* (Newman).

Artificially induced twinning always produces monozygotic twins (derived from one fertilized egg), while natural twinning, both habitual and sporadic, may be either monozygotic or multizygotic (derived from two or more fertilized eggs).

In mammals, for example, the recurring phenomenon of twinning by polyembryony (diplo- or polygenesis of one fertilized egg) is less frequent than another gemellogenetic mechanism—the simultaneous conception, gestation and birth of two or more individuals deriving from different fertilized eggs. The term "polyovulation" describes the simultaneous production of two or more fertilizable eggs.

Genetically, twins of a polyembryony, being derived from a single zygote, are called monozygotic (MZ) and are regarded as bearing an identical hereditary endowment. Twins deriving from polyovulation, and therefore from different zygotes, are called dizygotic (DZ) and are not regarded as carrying an identical heritage, but rather as being only partially alike. Two, three, or more individuals born at the same time, from a corresponding number of zygotes, are multizygotic.

These two mechanisms are present among the different species in varying proportions —normal, rare, or a combination—even in the same pregnancy. Polyovulation may also take place through a specific or sporadic mechanism of generation, as may be seen by the following table:

Among placental mammals the most characteristic and instructive example is afforded by the Xenarthri, where polyembryony is physiological—the production of more than one individual from the same fertilized egg being the usual means of generation and delivery.

The Xenarthri include certain species of armadillos which have a thick body covered with a layer of bony scales and horny blades, immobile in the shoulder and pelvic regions, but mobile in the central area where there are a number of independently mobile rings. These creatures live alone in tunnels dug out by themselves, emerging only to find food, which consists mainly of ants and other insects.

In 1894 Brehm, in his treatise on animal life, wrote as follows about the armadillo: "It is difficult to tell the sex of the young; this is why the Brazilians believe that the individuals born at the same time all have the same sex." This belief, related by the naturalist with evident skepticism, happens to be true and the Brazilian natives are correct in their assumption.

In 1885 v. Ihering discovered that the *Dasypus hybridus* of Brazil and Patagonia normally gives birth at the same time to eight offspring of the same sex. The author assumed this phenomenon was due to the splitting of a single fertilized egg by the usual twinning mechanism. In 1903, Cuénot

Gemellogenesis in the Animal Kingdom

- By polyembryony, i.e. monozygotic (MZ)
  - natural
    - specific
    - sporadic
  - artificial
- By polyovulation, i.e. dizygotic (DZ) or multizygotic
  - specific
  - sporadic

also studied the ovary of the armadillo with respect to the origin of twins.

However, it was work done by Newman and Patterson (1909) that threw light on the mechanism in the *Dasypus novemcinctus* (or Tatusia) species of Texas (Fig. 16) whereby four twins of the same sex were produced in a single birth. No more than one egg has ever been found in the female genital apparatus. Morever, it does not begin segmentation immediately after fertilization. Instead it remains in a static condition for about three weeks before undergoing the usual processes of morulation and blastulation. During gastrulation, however, the changes taking place assume a particular individuality, as may be seen in Figure 17. In the germinal vesicle, the embryonic node is first developed in the usual way. Then the progressive differentiation of an ectoderm and an entoderm begins. A cavity formed in the ectoderm represents the amnion. The ectodermic cells gradually migrate to the pole opposite that of the future placental attachment, grouping themselves into four germinal figures, one in each quarter formed by intersecting meridians.

In time, the four embryos derived from these figures move towards the point of placental insertion in the egg, retaining contact with the amniotic cavity. The embryos continue to grow, adhering to the wall of the original germinal vesicle, close to one another and joined to the same placenta but contained in separate cavities of the amnion (see Figs. 18 and 19). The newborn of a single pregnancy are of the same sex and extremely alike. Lane (1909) and Strahl (1913, 1914, 1917) also made contributions to the knowledge of polyembryony in the Tatusia.

Simultaneously with the discoveries of Newman and Patterson, but independently of them, Fernandez (1909), continuing v. Ihering's work on the *Dasypus hybridus*, demonstrated that natural polyembryony is a common event in this species, too. "I have discovered," he wrote, "that from the egg of the *mulita* (*Dasypus hybridus*) a germ is first formed consisting of two primitive blastodermic folds. This germ can in no way be distinguished from the embryos at the same stage in other vertebrates; but from seven to twelve embryos deriving from this single germ soon start taking shape."

Regarding other species of Xenarthri, so far as is known today, polyembryony does not exist. For example, the *Euphractus villosus* regularly gives birth to two offspring, but they are not derived from the same egg and may also be of opposite sex, as Fernandez found in seven out of the ten cases studied.

Goats

Among goats, according to Wehefritz (1925), twinning occurs in 75 per cent of all births, and, as noted by Mackens, triplets are also frequent. Butz (1932) tried the similarity method including such tests as skin grafts and ECG on two pairs of twin goats—one pair male MZ and the other female MZ. The twins were alike in dimensions, weight, and the qualities of their fur. Butz also found in the goat two bicephalous monsters showing signs of mirror-imaging.

Patt (1938) mentions a quintuplet delivery by a goat that had itself been born in one of four multiple deliveries by its mother (three triplet births and one quintuplet). Also, the *Journal of Heredity* reported quintuplets delivered by a milking goat fertilized by a male which had previously fathered two sets of quintuplets. Reproduced in Figure 20 is a photograph of the father, the mother and their five young, christened "The Dionne quins in the caprine family" by the *Journal*.

Biegert (1938) showed that climate has

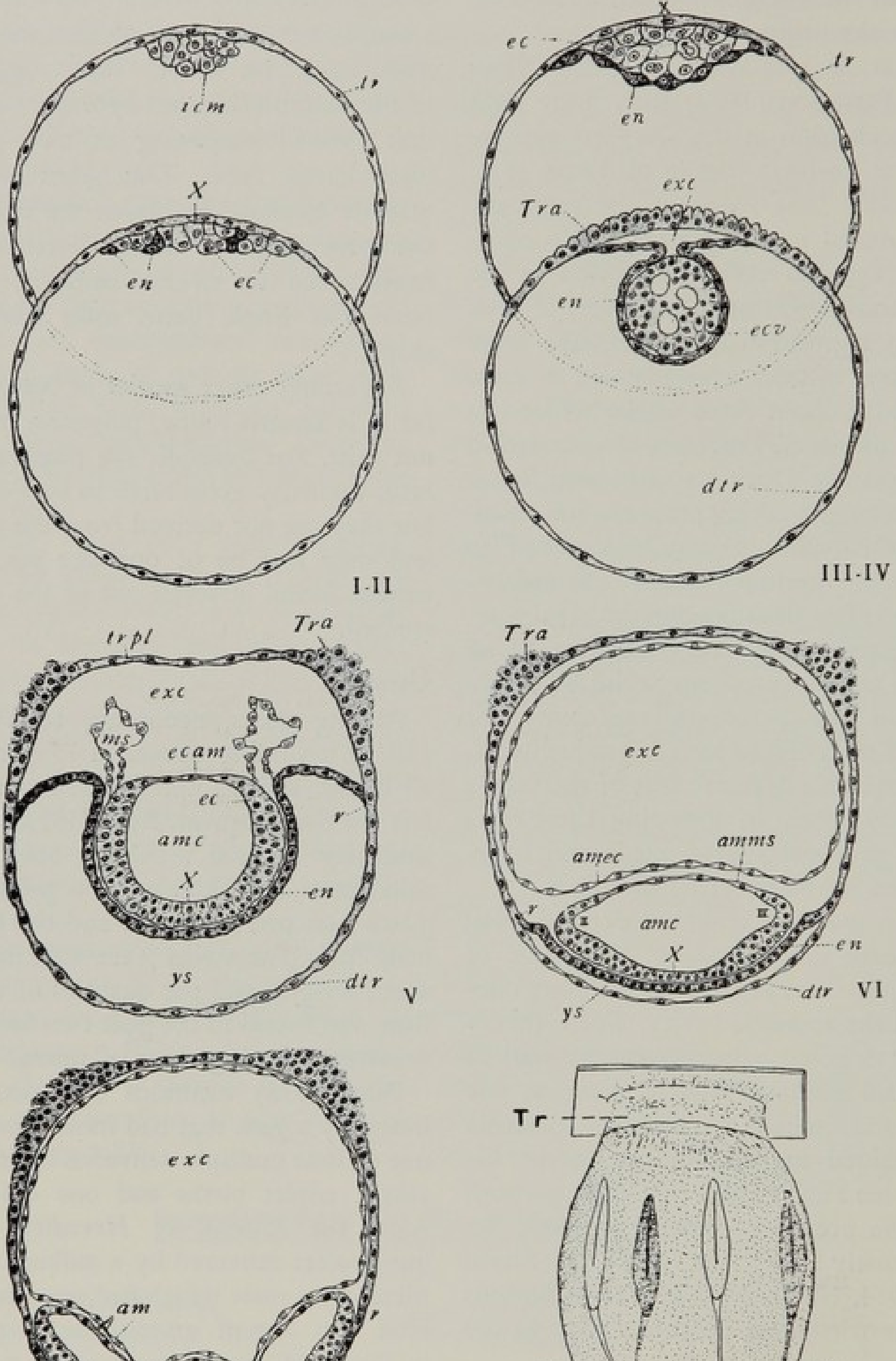


Fig. 17. Embryonic development of the *Dasypus novemcinctus Texanus* (Newman).

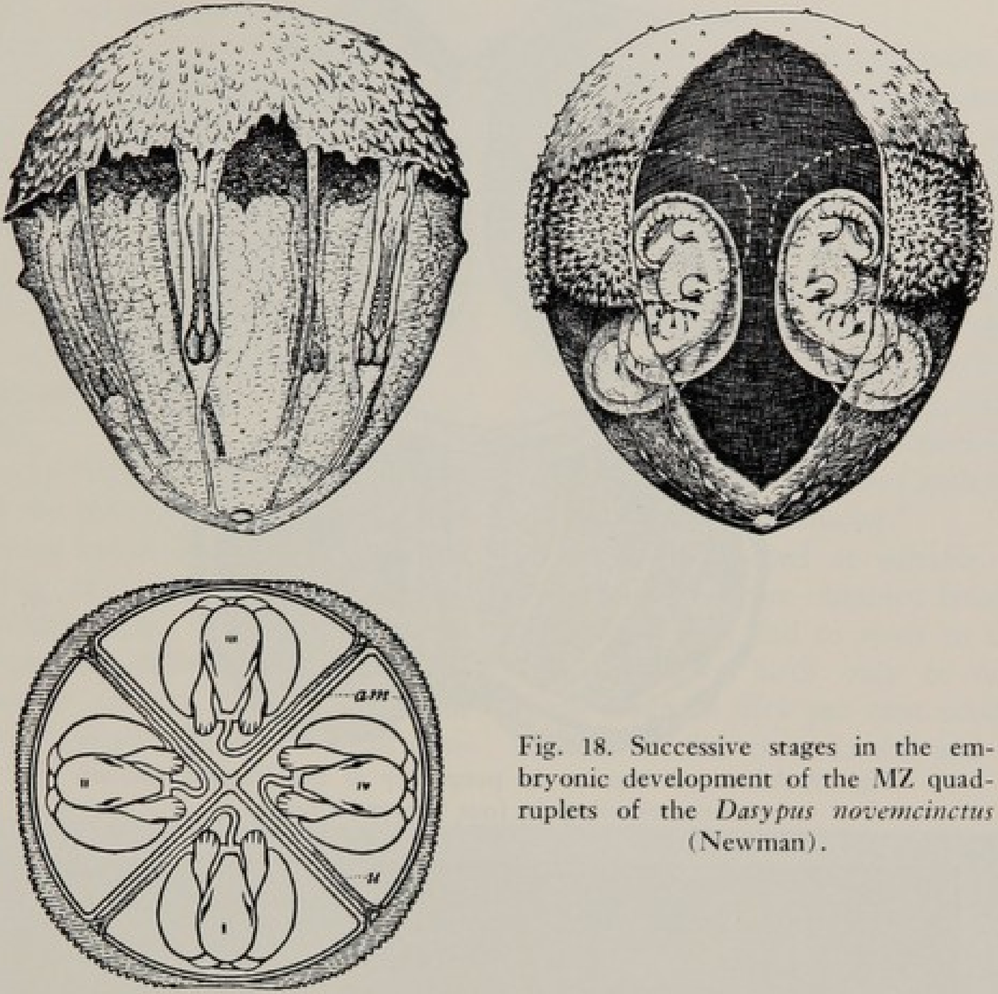


Fig. 18. Successive stages in the embryonic development of the MZ quadruplets of the *Dasypus novemcinctus* (Newman).

a decided influence on multiple births in the goat, with a cold rainy summer increasing the number of twin births, and a hot dry one diminishing it. Van Steenkiste (1845) and Bien (1905) each described some cases of double monstrosities, and v. Weber (1944) reported a pair of DZ unifollicular twin goats.

Sheep

In the year 1889, and for more than a quarter of a century thereafter, Bell tried by cross breeding to obtain sheep with more than two nipples (six to eight) which might produce twins more frequently and at an earlier age than ordinary sheep. There appeared to be some connection between these two factors. During his experiments, Bell noted the importance of certain exogenous factors in determining an increase in multiparity: (1) Maturity of the sheep—four-, five- and six-year-olds producing twins more frequently than younger or older sheep. (2) Mating in October, and subsequent parturition in March. (3) Rapid increase in weight at the time of mating and subsequent loss of weight. (Bell is said to have succeeded in obtaining an increase in twin births by overfeeding the sheep before mating.)

Marshall gives an account of a sheep breeder who managed to obtain two hundred offspring from ten sheep through a continuous selection of twin-producing Hampshiredown sheep. Von Patow, by his studies on certain merinos flocks bred for

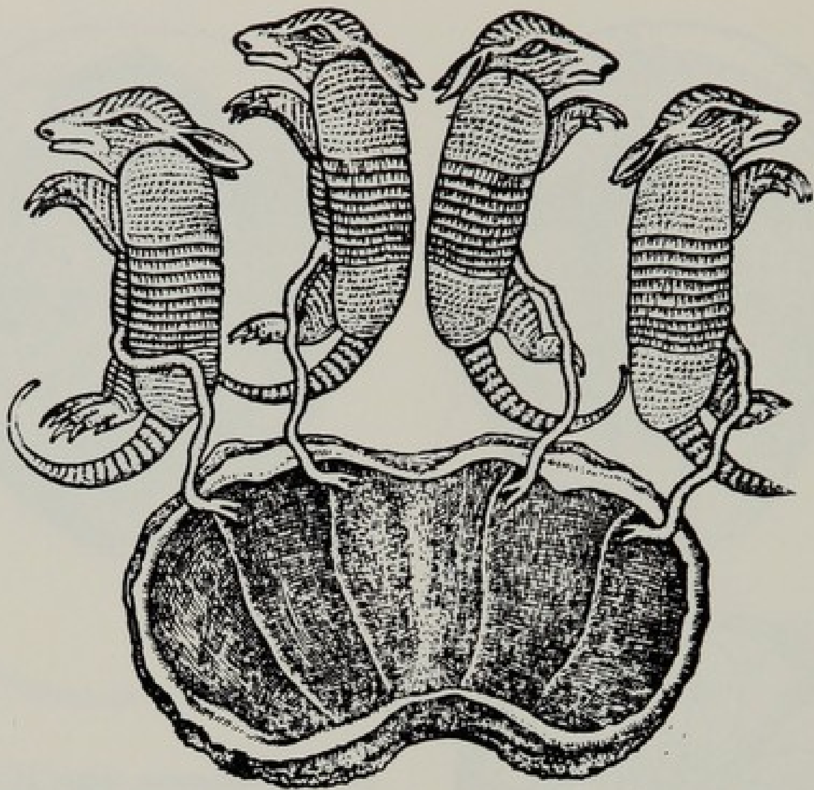


Fig. 19. Advanced stage in the pregnancy of the *Dasypus novemcinctus* showing the four fetuses (Newman).

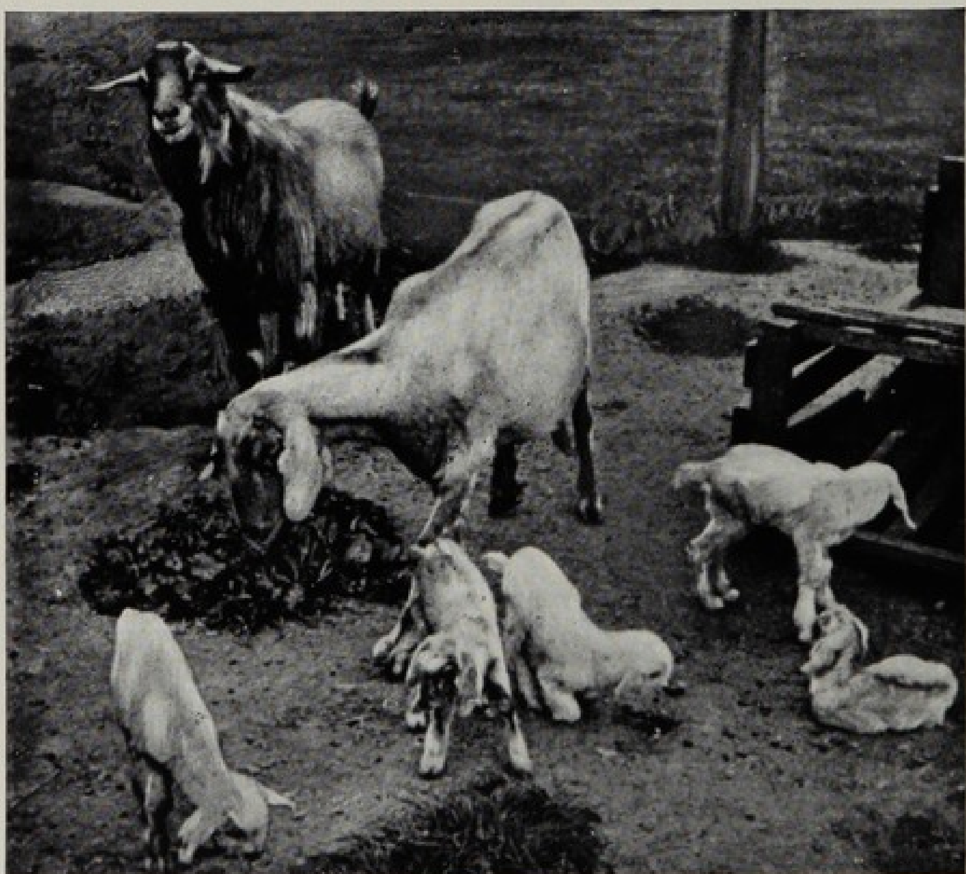


Fig. 20. Five kids born from the same goat (from the *Journal of Heredity*).

slaughtering, was able to affirm that environment and, more importantly, different types of nutrition may condition twinning among sheep. Insufficient feeding during the first World War resulted in decreased fecundity, sometimes reducing the lambs to one in every delivery. This theory is also supported by Zuckermann (1937) who reported that breeders are well aware that abundant nutrition stimulates fecundity in sheep, thereby increasing the number of twin births.

Wilson and Gregory (1931) reported on a sheep of the Romney breed which delivered six living lambs, three males and three females (Fig. 21). Aubel (1932) observed a sheep which, after three normal pregnancies, separately delivered three lambs in a total period of 211 days. The author thought this case was probably one of double superfetation.

In the Soviet Union extremely practical as well as interesting studies were initiated by Zawadowsky in 1941, based on a hormonal method of stimulating twinning in sheep. As reported by Caullery, who visited Moscow in 1945, Zawadowsky's school is regularly able to produce two deliveries a year, or three in two years, by stimulating with hormonal injections the ovary of the sheep during the summer when this gland is at rest. In addition, a considerable multiparity has been attained, as Caullery puts it, by "experimental twinning."

Of sheep injected at suitable intervals with doses of serum obtained from a pregnant mare, 43% fail to react to the treatment and give birth only to one lamb. Forty-seven to fifty per cent produce two lambs, 6 to 8% three lambs, and 1 to 2%

Fig. 21. Six lambs born from one sheep (Wilson and Gregory).

deliver four, five and even six lambs. In this way, the natural multiparity of the species is considerably increased.

Zawadowsky's experiments were first carried out on the Karakul breed, which produces astrakhan, and then on other breeds (the fat-tail, the strigai, précos, merinos, rambouillets and their hybrids). By varying the dose, the degree of superfecundity may be regulated. The sheep withstand the treatment with no ill effects, even if repeated for several years. The lambs of multiple pregnancies are easily raised and after about a year and a half weigh the same as those born singly.

The method proved most profitable and by 1945 several million sheep had been injected with pregnant mare serum, prepared in large quantities in Central Asia (Kazakhstan, Uzbekistan, Turkmenistan) and in special laboratories in the Northern Caucasus. In order to persuade the shepherds to have their sheep so treated, Zawadowsky wrote a description and instruction for them in the *Life of a Shepherd*. Not only is the method of considerable scientific value but it is also a fine example of commercialization of animal twinning.

Bovines

Bovine animals (artiodactyle ungulates) are generally uniparous, but twins are not uncommon and have served as the object of many significant studies. The annual variability in the production of twins is believed to be due chiefly to exogenous circumstances, such as the season during which copulation took place, feeding, and intensity of solar irradiation (Johansson, Thomas, Marwitz, Löwe and Ruthart). W. v. Weber, who in 1944 observed the considerable yearly fluctuations represented in the graph in Figure 22, acknowledged the presence of a hereditary component, since there is obviously a greater activity on the part of the more decidedly gemelliparous stocks in the years of greater proliferation.

Thorough investigations were carried out on bovine twins in the *Institut für Tierzüchtung und Haustiergenetik* of the *Friederich Wilhelms-Universität* of Berlin by Kronacher (1930, 1932), who studied 35 pairs and worked out a system like that of Siemens-v. Verschuer for human twins. By this method an observer could determine whether a pair was monozygotic or dizygotic, on the basis of similarity of many quantitative and qualitative characteristics, such as the shape of the body, weight, pattern of the fur, papillary nodules on the nose, texture of hair, dentition, production of milk, composition of the blood, blood groups, and even certain qualities of intelligence (Figs. 23-26).

It should be noted that the twins examined by Kronacher were of the same sex in each pair, with five pairs diagnosed MZ, nine doubtful, and 21 DZ. The MZ twins would represent 1% of all bovine twins. According to Kronacher, the diagnosis of ovularity may be strengthened when *corpora lutea* are found on inspection of the ovary of the maternal cow following delivery. However, the presence of the *corpora lutea* is not absolutely decisive, because even a single *corpus luteum* may result from a follicle containing two eggs, though in many cases a complete correspondence of characteristics in two calves has been found to be associated with a single *corpus luteum.*

Kronacher compiled a list of cases of twins occurring in domestic animals reported in the literature up to the year 1932, classifying them according to age and sex. He stated that the majority of ruminant twins are of dizygotic origin and may be of the same or of opposite sex. Further, he pointed out that the study of twins in domestic animals is also relevant in the study

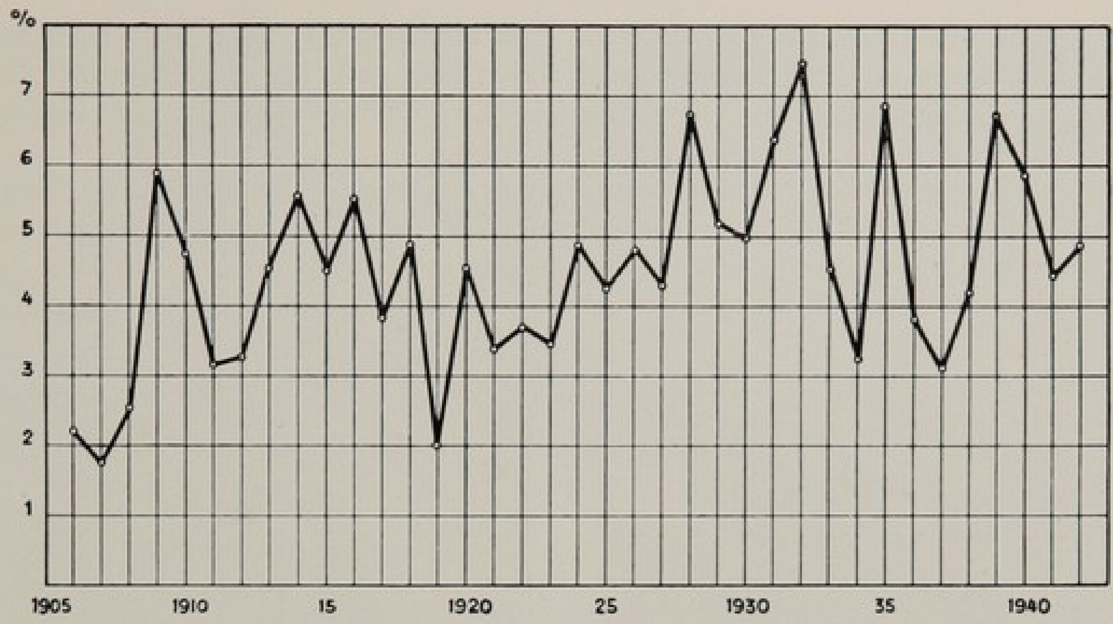


Fig. 22. Annual variability in the frequency of twin births in Zimmerwald cows between 1906 and 1942 (W. v. Weber).

of human twins.

In 1940, Vieth described a typical case of superfecundation in a Guernsey cow. Having copulated twice, once with an Angus bull and again with one of the Hereford breed, it had a twin pregnancy which resulted in two females—one bearing the characteristics of the Angus, and the other those of the Hereford breed (Fig. 27).

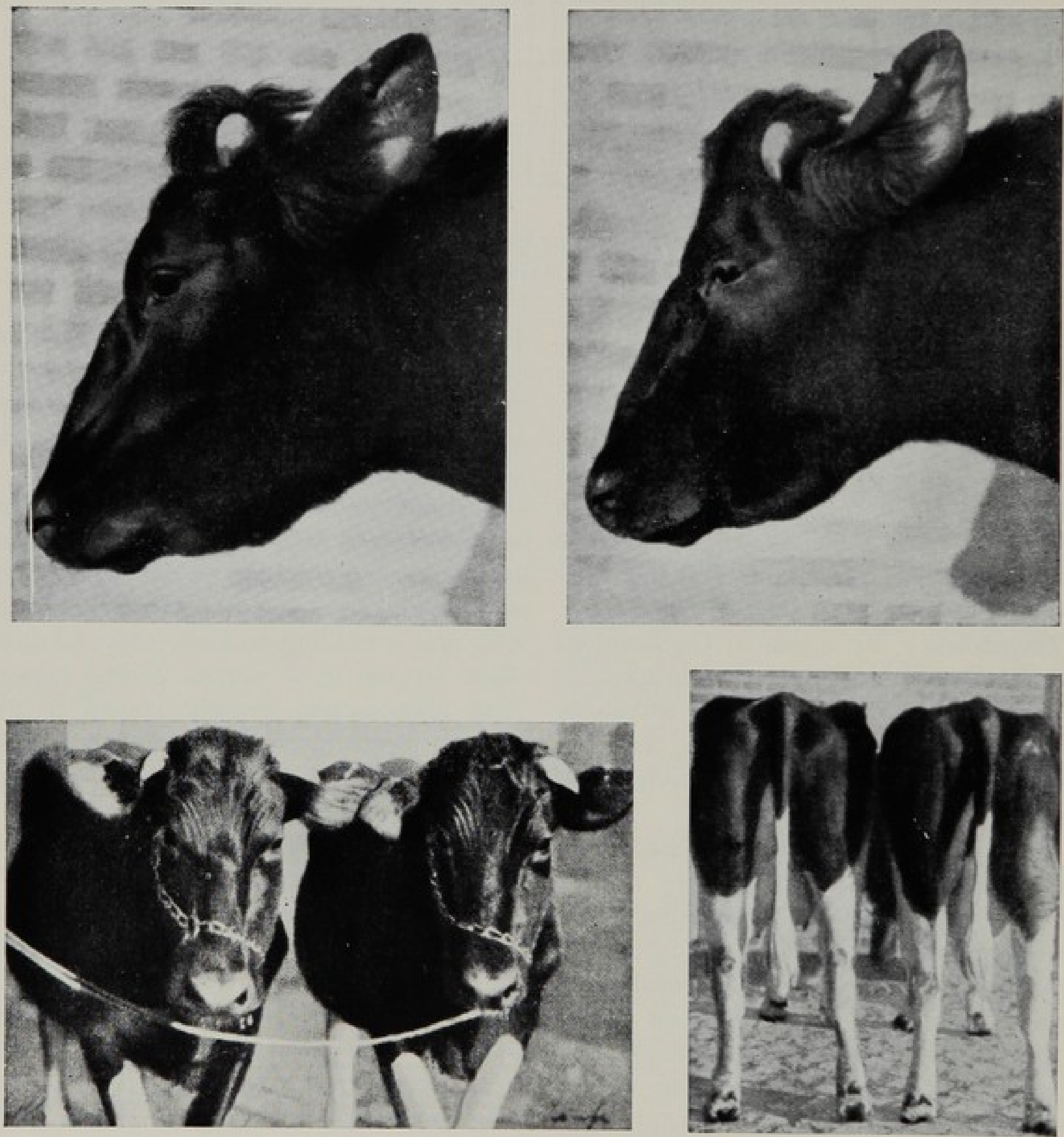
Zawadowsky, by means of the hormone treatment with which he experimented so successfully on sheep, was able to greatly increase gemelliparity in the cow, obtaining 145 calves from 100 cows in double, triple and even quadruple deliveries.

W. v. Weber (1944-45) published data on the frequency and hereditary components of twin births in simmenthal cows. Using the information in books dealing with 40 years of Zimmerwald cattle breeding, the author based his conclusions on 10,104 births, including 466 twin, 11 triplet and 2 quadruplet births. According to Weber, the frequency of twins is dependent on the age of the mother, with the peak reached by the eighth or ninth pregnancy. However, the author pointed out that final conclusions could only be drawn if the mother cows were to arrive at an age equivalent to that of the human climacteric (Fig. 28).

It should be noted that in DZ twin calves of different sex, the male is usually normal but its cotwin is nearly always a hermaphrodite (Fig. 29). According to Keller, only 6%, and according to Luer only 5.3% of these females show normal genital organs. The phenomenon, already known to the ancient Romans, who called these sterile females *taura,* was studied by the American scientist Lillie (1917), who gave the term "freemartin" to these sterile twins and offered an explanation of the cause. He attached great importance to the fusing of the fetal membranes of the two cotwins through arterial anastomoses (Fig. 30), which, by the mixing of the two blood streams, produces a precocious parabiosis.

In two instances Lillie observed the anastomoses between embryos 5 mm. long, and 3 mm. wide, and came to the conclusion that, in freemartinism, substances produced by the gonads of the male embryo directed the process of sexual inversion in the female embryo. Also, Lillie believed the sooner the anastomosis took place, the greater the masculinization. Lesbouyries (1949) pointed out that this masculinization of the female gonad may be verified histologically. The successive stages in the evolution of this teratological gonad have been studied by Lillie and his collaborators, Chapin (1917), Willies (1921), and Bissonnette (1928).

According to Lesbouyries, no feminization of the male embryo by the female blood ever occurs, partly because of the earlier differentiation of the testicle (Van



Figs. 23-26. Several views of a pair of MZ cows (Kronacher).

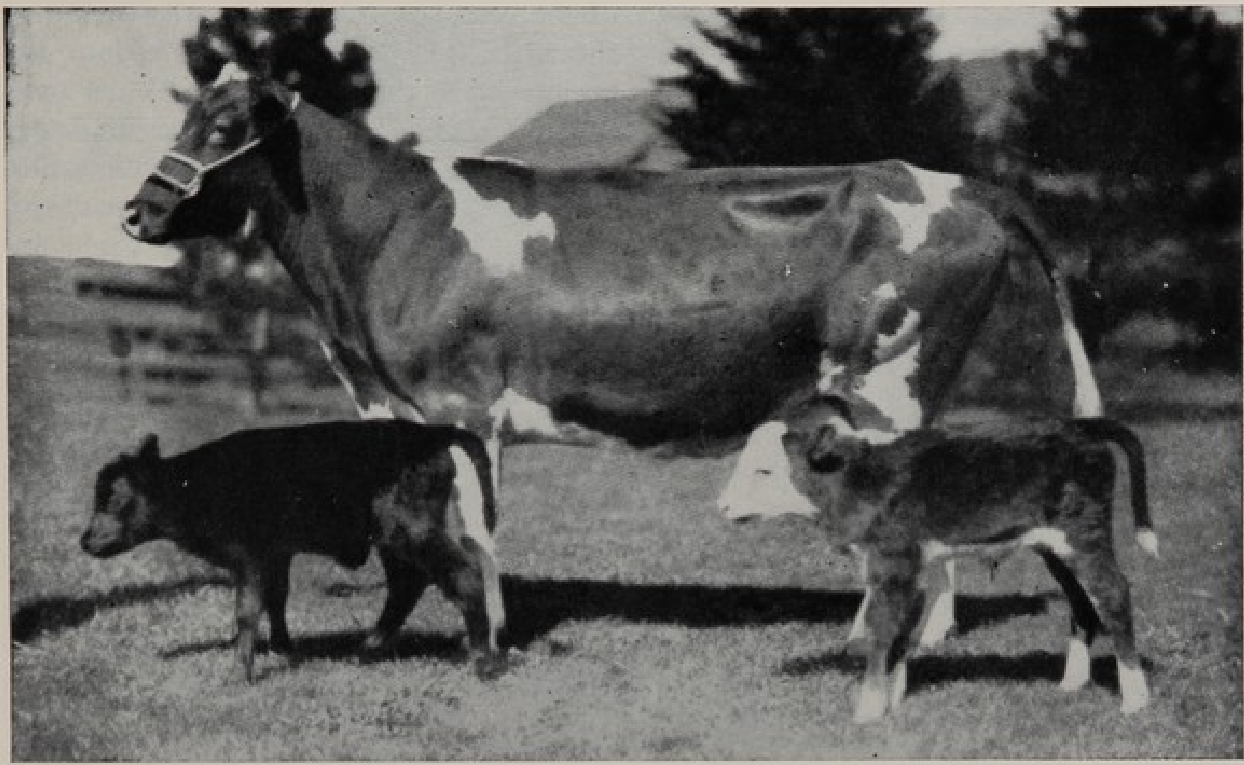


Fig. 27. Mother cow with female twin calves; case of superfecundation by two bulls of different breeds (Vieth).

Fig. 28. Frequency of bovine twin births according to order of birth (W. v. Weber). (Geburt = Order of birth.)

Beck, 1926), which is already apparent when the embryo is only 19 mm. long, but chiefly because of the precocious differentiation of the male interstitial gland when the embryo has grown to 30 mm. Differentiation of the interstitial endocrine elements of the ovary only occurs at the of the vascular arch, i. e., by the timing of the male hormone's penetration into the circulation of the female twin. When anastomosis is established soon after implantation of the egg, a strong masculinization takes place with formation of a peniform clitoris. This observation was made by

Fig. 29. Freemartin (Tammeo).

82 mm. stage (Bascom, 1923). On histological examination the ovaries of a 38 mm. freemartin embryo show a hypoplasia of the cortical formations, indicating an evolution of the gland towards the male type. At this stage, vascular anastomosis is already clearly visible, although it appears only in a fine capillary arch.

The different types of sexual mosaic found in the freemartin can be explained by the more or less precocious formation

Keller in a fetus of five months, by Roberts and Greenwood (1928) in the adult, and by Buyse in a freemartin, born together with two other normal male twins, which possessed a peniform clitoris 26 cm. long.

The freemartin is therefore a hermaphrodite or a pseudohermaphrodite of purely hormonal origin, since the phenomenon cannot be explained on grounds other than the vascular anastomosis. Freemartins may

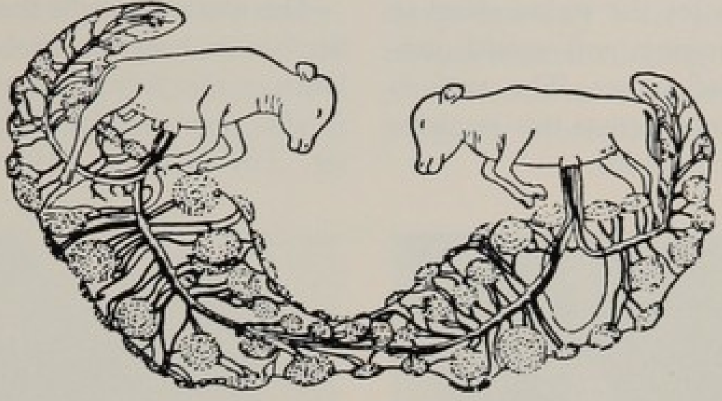


Fig. 30. Twin pregnancy, the two embryos being of different sex and their placentae united (Lillie).

be used for work, like oxen, but are generally unsuited for reproduction and milking.

Monkeys

On the subject of sporadic twinning among monkeys, Abel (1933) describes a rare case of twins born to an African (Paviana) monkey in the zoological gardens of Berlin. The twins were stillborn. Their measurements and other data obtained by the author were insufficient for a diagnosis of mono- or dizygosity. The fetal membranes, which might have facilitated the diagnosis, had been eaten by the mother, as is customary with monkeys.

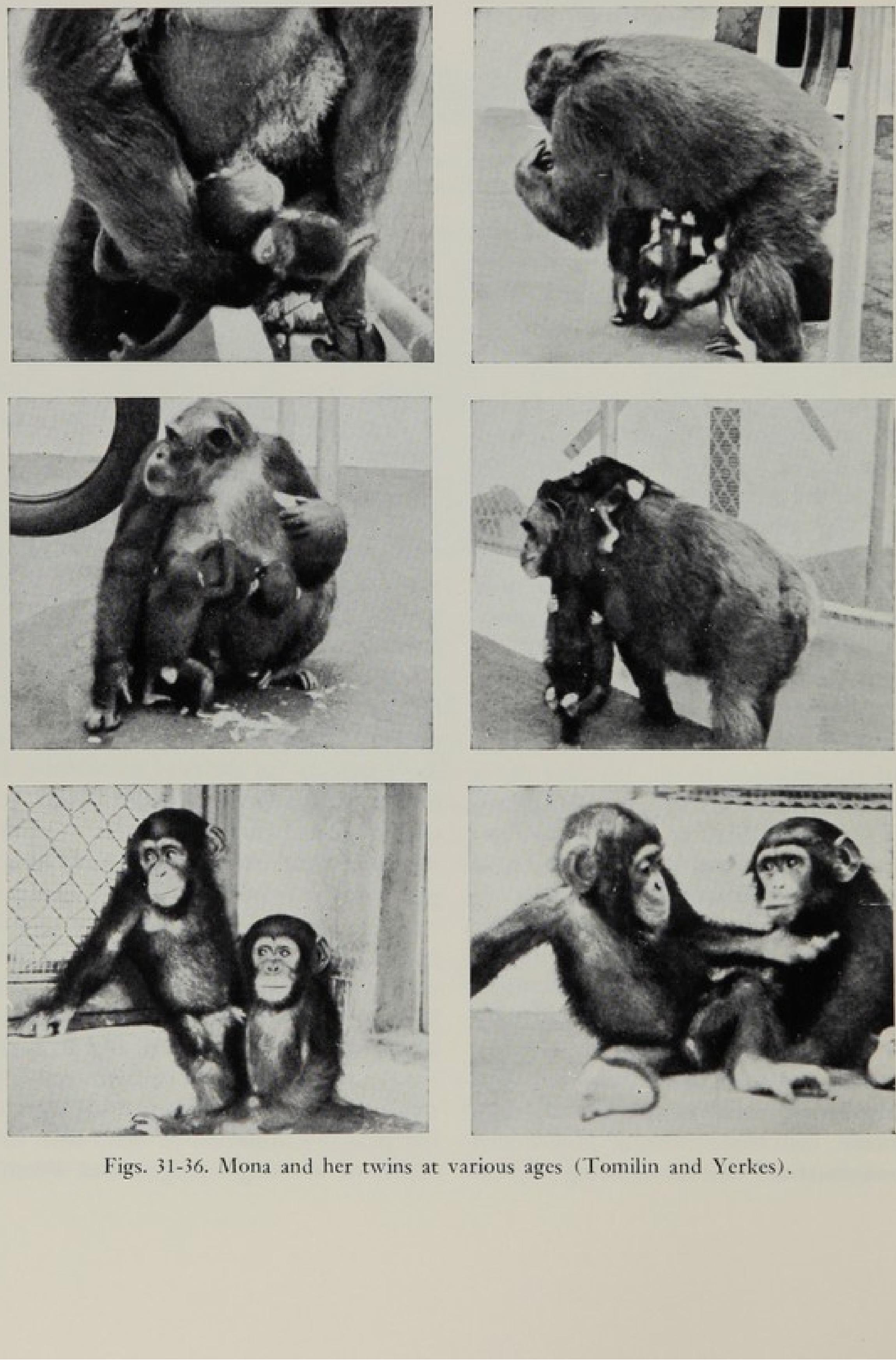
In 1934, Yerkes reported the birth of a pair of opposite-sex twins delivered by a female chimpanzee in 1933 at the Anthropoid Experiment Station of Yale University. Later, Tomilin and Yerkes (1935) gave a more detailed description of this twin birth, which they considered to be the only multiple birth ever observed among anthropoids. These twin chimpanzees were also studied from a somatometric point of view by Jacoben and Yoshioka.

The father, Pan, was 11 years old. The mother, Mona, who was about 20, had previously had three normal pregnancies and one abortion. On the morning of June 26, 1933 it was found that she had given birth to a pair of twins. According to the authors' estimates, the period of gestation was 210±5 days, or seven and a half lunar months. The afterbirth disappeared before the observer arrived, presumably eaten by Mona.

The twins were named Tom and Helene. Though apparently physically normal at birth, they were thin, weak and small, perhaps because of their premature birth. Each weighed about 1,500 gm., and they were approximately the same in size. The color of their eyes, however, was different. The female grew more rapidly in the first six months, after which the male developed more quickly for the next six months. Tom began eating supplementary foods at an earlier age and with greater zest. When they were one year old, the male weighed 5,880 gm. and the female 4,320 gm.

The twins' temperament was very different. Tom was active, independent, adventurous, fearless, aggressive yet docile. Helene was more attached to her mother, unaggressive, timid, fearful but difficult to handle and obstinate. The mother was particular about the cleanliness of her twins, but paid less attention to them than to the babies of her single pregnancies. From the start she refused to let the twins cling to her while she was resting, and would punish them if they defied her. The authors had never before come across this punitive behavior among anthropoids.

The mother taught the twins how to find her breast, how to climb and how to walk. During the first few months she would fondle them whenever they appeared upset. Towards the end of the year her at-



Figs. 31-36. Mona and her twins at various ages (Tomilin and Yerkes).

tempts to wean the twins became evident. Nevertheless, she continued to suckle them until they were separated from her when only a little over a year old. It is interesting that when they were about 11 months old, Helene started running to her twin instead of their mother when she felt the need for refuge or protection (Figs. 31-36).

Chapter IV

FREQUENCY OF THE TWINNING PHENOMENON

1. FREQUENCY OF TWINS IN CENSUS RECORDS

PRESENT-DAY BUREAUS of vital statistics, in all the civilized countries of the world, make available to us accurate figures on the frequency of the twinning phenomenon. However, even before statistics were provided as a matter of course by governments, as they are today, records of births were kept in parishes, townships, and various institutions, so that from the time the biological sciences first became interested in twins, it was possible for research workers to gather figures on their frequency and attempt to interpret them.

EUROPE

The work done by the International Institute for Statistics in The Hague has enabled us to study the frequency of the twinning phenomenon in many countries of the world, based on fairly recent, detailed and easily comparable data. In Europe, only those countries with a more characteristic occurrence of twins are mentioned here. Statistical information, unless otherwise indicated, has been obtained from the *Aperçus de la démographie des divers Pays du monde*, while the statistical elaboration—averages, ratios, indices—is our own. As far as possible, we have focused our attention on figures referring to the decade midway

Table I

DENMARK

Year	*Number of Births*			*Multiple Births in Every 1000 Deliveries*	*Single Births for Every Multiple Delivery*
	Single	*Multiple*	*Total*		
1926	70,043	1,160	71,203	16.3	60
1927	67,394	1,109	68,503	16.2	61
1928	67,980	1,081	69,061	15.7	63
1929	64,703	1,102	65,805	16.7	59
1930	65,701	1,091	66,792	16.3	60
1931	63,854	987	64,841	15.2	65
1932	64,097	1,032	65,129	15.8	62
1933	62,523	957	63,480	15.1	65
1934	64,734	1,038	65,772	15.8	62
1935	64,746	1,072	65,818	16.3	60
Average	65,577	1,062	66,640	15.9	61.7

Table II

SWEDEN

Year	*Number of Births*			*Multiple Births in Every 1000 Deliveries*	*Single Births for Every Multiple Delivery*
	Single	*Multiple*	*Total*		
1926	101,496	1,576	103,072	15.3	64
1927	97,685	1,424	99,109	14.4	69
1928	97,657	1,426	99,083	14.4	68
1929	92,491	1,443	93,934	15.4	64
1930	94,009	1,398	95,407	14.7	67
1931	91,132	1,280	92,412	13.9	71
1932	89,694	1,288	90,982	14.2	70
1933	84,984	1,175	86,159	13.6	72
1934	85,126	1,160	86,286	13.4	73
1935	85,897	1,184	87,081	13.6	73
Average	92,017	1,335	93,352	14.2	69

between the First and Second World Wars (1926-1935).

Denmark

According to these figures, Denmark comes first with the greatest frequency of twinning in Europe. It should be noted that in an earlier period (1901-1910), described by March, Denmark followed Sweden and Bulgaria in order of frequency. (See Table I.)

Sweden

Though Sweden had a frequency of 15 twin births in every 1,000 deliveries chosen at random from 1901-1910, on the basis of the 1926-1935 figures Sweden's frequency is somewhat diminished (14.2). As will be noted in the figures for each year given in Table II, a progressive reduction of frequency has taken place.

Scotland

These figures may be taken as an indication of the frequency of the phenomenon in Great Britain. It should be noted that stillborn children have been excluded, the delivery being considered multiple only if there are at least two living infants. (See Table III.)

Germany

Up to 1934, births occurring in the Saar were not included. While Lotze observed in 1937 that statistics covering a period of many years showed a frequency of one twin delivery in 85 births in Germany, our own data indicate a higher frequency (one in 81.6). We may therefore assume that there has been a slight increase in frequency. (See Table IV.)

Italy

In 1914, Patellani studied multiparity in Italy by calculating the number of deliveries recorded in 43 years (from 1872 to 1914)—a total of 47,782,180, of which 565,-176 were multiple births. On this basis, he

Table III

SCOTLAND

Year	*Number of Births*			*Multiple Births in Every 1000 Deliveries*	*Single Births for Every Multiple Delivery*
	Single	*Multiple*	*Total*		
1926	99,854	1,291	101,145	12.8	77
1927	94,171	1,246	95,417	13.1	76
1928	94,375	1,216	95,591	12.7	78
1929	90,530	1,169	91,699	12.7	77
1930	91,992	1,274	93,266	13.7	72
1931	89,941	1,132	91,073	12.4	79
1932	88,737	1,123	89,860	12.5	79
1933	84,382	1,077	85,459	12.6	78
1934	86,723	1,049	87,772	12.0	83
1935	85,797	1,063	86,860	12.2	81
Average	90,650	1,164	91,814	12.6	78

Table IV

GERMANY

Year	*Number of Births*			*Multiple Births in Every 1000 Deliveries*	*Single Births for Every Multiple Delivery*
	Single	*Multiple*	*Total*		
1926	1,239,156	15,056	1,254,212	12.0	82
1927	1,171,070	14,402	1,185,472	12.1	81
1928	1,191,430	14,604	1,206,034	12.1	82
1929	1,155,258	14,171	1,169,429	12.1	82
1930	1,135,880	13,689	1,149,569	11.9	83
1931	1,037,908	12,944	1,050,852	12.3	80
1932	983,897	11,893	995,790	11.9	83
1933	961,356	11,789	973,145	12.1	82
1934	1,185,223	14,777	1,200,000	12.3	80
1935	1,265,828	15,551	1,281,379	12.1	81.0
Average	1,132,700	13,887	1,146,588	12.0	81.6

arrived at the following figures: one multiple birth in 84.54 deliveries, chosen at random; one multiple birth in 83.54 single deliveries.

Also, he was able to show that multiparity is most frequent in the lower Po Valley in the provinces of Rovigo and Ferrara (one multiple birth in 54-54.3 single births) with infiltrations into the neighboring provinces of Venice, Padua, Ravenna, Bologna and Forlì.

Multiparity is at a minimum in the provinces of Catanzaro and Reggio Calabria (one multiple in every 129.1-126.8 single births), and also in the provinces of Salerno, Messina and Cosenza. All in all, the frequency of multiparity, as compared with uniparity, is distributed in the following manner in Italy: Northern Italy 1:73; Central Italy 1:79; Southern and Insular Italy 1:102. The map in Figure 37 shows the distribution of twin births in various regions. (See Tables V and VI.)

Table V
ITALY

Year	*Number of Births*			*Multiple Births in Every 1000 Deliveries*	*Single Births for Every Multiple Delivery*
	Single	*Multiple*	*Total*		
1926	1,112,482	12,944	1,125,426	11.5	86
1927	1,108,165	13,667	1,121,832	12.2	81
1928	1,086,171	12,847	1,099,018	11.7	85
1929	1,049,611	13,081	1,062,692	12.3	80
1930	1,101,430	15,478	1,116,908	13.9	71
1931	1,034,125	14,160	1,048,285	13.5	73
1932	998,574	13,569	1,012,143	13.4	74
1933	1,002,820	14,145	1,016,965	13.9	71
1934	1,000,113	13,523	1,013,636	13.3	74
1935	1,002,679	13,859	1,016,538	13.6	72
Average	1,049,617	13,727	1,063,344	12.9	76.7

TABLE
DISTRIBUTION OF SINGLE AND TWIN

Regions	1931		1932		1933		1934		1935	
	Single Births	*Twin Births*	*Single Births*	*Twin Births*	*Single Births*	*Twin Births*	*Single Births*	*Twin Births*	*Single Births*	*Twin Births*
Piedmont	57,812	684	55,057	638	51,504	649	51,773	575	51,894	634
Liguria	22,703	257	22,077	271	21,100	235	20,790	250	20,835	241
Lombardy	124,839	1,671	122,366	1,668	117,121	1,672	118,012	1,649	119,912	1,698
Venetia Tridentina	14,480	196	14,186	226	13,752	214	13,625	176	13,785	214
Venetia	105,676	1,668	103,673	1,579	101,039	1,639	103,353	1,593	102,815	1,660
Venetia Jul. and Zara	19,507	255	18,693	234	18,368	282	18,440	264	18,880	304
Emilia	69,941	892	66,013	894	66,189	882	67,942	873	66,817	839
Tuscany	56,907	720	51,929	668	51,358	665	50,971	648	52,471	695
Marches	31,572	469	28,867	424	29,827	452	29,872	407	29,929	464
Umbria	17,409	267	15,756	210	16,157	242	16,005	224	16,100	243
Latium	60,966	887	58,481	787	59,752	879	61,775	821	63,306	852
Abruzzi and Molise	45,893	651	43,501	609	47,326	697	44,620	594	44,873	643
Campania	111,618	1,596	109,397	1,602	110,599	1,632	107,859	1,577	110,056	1,529
Apulia	82,990	1,116	80,755	1,073	81,233	1,109	82,239	1,118	82,446	1,172
Lucania	18,246	233	17,904	212	18,890	229	19,061	252	18,474	258
Calabria	54,929	723	55,099	691	57,411	720	54,636	623	55,439	689
Sicily	110,426	1,379	106,344	1,289	111,979	1,415	110,130	1,353	107,348	1,235
Sardinia	28,211	335	28,476	333	29,215	378	29,010	348	27,299	330
Totals	1,034,125	13,999	998,574	13,408	1,002,820	3,991	1,000,113	13,345	1,002,679	13,700

France

Bertillon provides the following information regarding the frequency in different sections of France. The lowest figures are found in the Southwest and the Central Plateau: Gironde, 6.77; Haute-Garonne, 7.03; Charente, 7.16; Gers, 7.59; Dordogne, 7.45; Corrèze, 7.06; Ardèche, 7.37; Lozère, 7.48; Cantal, 7.56; and Puy-de-Dôme, 7.95. The highest figures are found in the regions of Savoie, Jura, Vosges and Bretagne: Haute-Savoie, 12.90; Savoie, 12.80; Jura, 11.37; Vosges, 11.84; Moselle, 12.41; Vendée, 12.34; Morbihan, 11.43; Finistère, 11.36. The map drawn by Turquan (Fig. 38) gives a clear picture of the distribution in France. (See also Table VII.)

Table VII

FRANCE

Year	*Number of Births*			*Multiple Births in Every 1000 Deliveries*	*Single Births for Every Multiple Delivery*
	Single	*Multiple*	*Total*		
1926	778,819	8,348	787,167	10.6	93
1927	753,574	8,300	761,874	10.9	91
1928	758,875	8,515	767,390	11.0	89
1929	739,268	8,062	747,330	10.8	92
1930	759,422	8,256	767,678	10.8	92
1931	743,969	7,788	751,757	10.4	96
1932	736,665	8,067	739,596	10.9	91
1933	687,226	7,622	694,848	11.0	90
1934	686,212	7,447	693,659	10.7	92
1935	648,310	7,046	655,356	10.8	92
Average	728,720	7,945	731,529	10.7	91.8

Spain

(See Table VIII.)

VI

BIRTHS IN ITALY (1931-1940)

1936		1937		1938		1939		1940		*Total Single Births*	*Total Twin Births*	*Ratio of Twin Births to 1000 Single Births*
Single Births	*Twin Births*	*Single Births*	*Twin Births*	*Single Births*	*Twin Births*	*Single Births*	*Twin Births*	*Single Births*	*Twin Births*			
50,070	585	52,509	607	56,129	621	54,455	627	53,319	646	534,522	6,266	11.72
20,341	239	21,707	278	23,182	270	22,337	279	22,027	267	217,099	2,587	11.91
114,327	1,562	120,579	1,702	128,842	1,722	127,963	1,734	127,316	1,747	1,221,277	16,825	13.77
13,349	216	14,039	197	15,090	215	14,968	198	14,833	216	142,107	2,068	14.55
98,843	1,585	101,443	1,561	105,676	1,644	104,358	1,688	104,726	1,586	1,031,602	16,203	15.70
18,109	254	19,106	262	20,196	296	20,234	299	20,765	269	192,298	2,719	14.13
61,155	771	64,236	798	68,502	886	65,713	848	64,815	799	661,341	8,482	12.82
50,080	611	51,934	648	56,384	680	53,575	688	54,844	691	530,453	6,714	12.65
28,111	450	29,725	393	30,993	437	29,825	426	28,465	376	297,186	4,298	14.46
15,366	190	16,089	233	17,320	231	16,084	243	16,286	234	162,572	2,317	14.25
61,612	848	64,662	910	68,284	925	68,528	941	69,853	893	637,219	8,743	13.70
43,137	594	44,036	619	41,574	547	43,749	625	42,544	587	443,253	6,166	13.91
106,059	1,510	108,348	1,661	110,825	1,648	115,023	1,807	115,402	1,644	1,105,186	16,206	14.66
80,113	1,106	83,169	1,089	85,218	1,190	87,625	1,235	87,885	1,143	883,693	11,351	12.84
18,071	234	18,780	242	18,043	247	18,835	250	18,380	248	184,684	2,405	13.02
54,867	639	53,764	655	55,182	706	56,979	778	57,500	755	555,806	6,979	12.55
104,785	1,360	103,871	1,340	111,136	1,424	111,152	1,470	116,608	1,519	1,093,779	13,784	12.60
29,754	391	28,843	376	30,269	351	32,741	455	34,619	412	298,437	3,709	12.42
968,149	13,145	996,840	13,571	1,042,845	14,040	1,044,144	14,591	1,050,187	14,032	10,192,514	137,822	13.52

Fig. 37. Frequency of twin births in Italy. Shaded areas represent number of twin births per 1,000 single births (see key above).

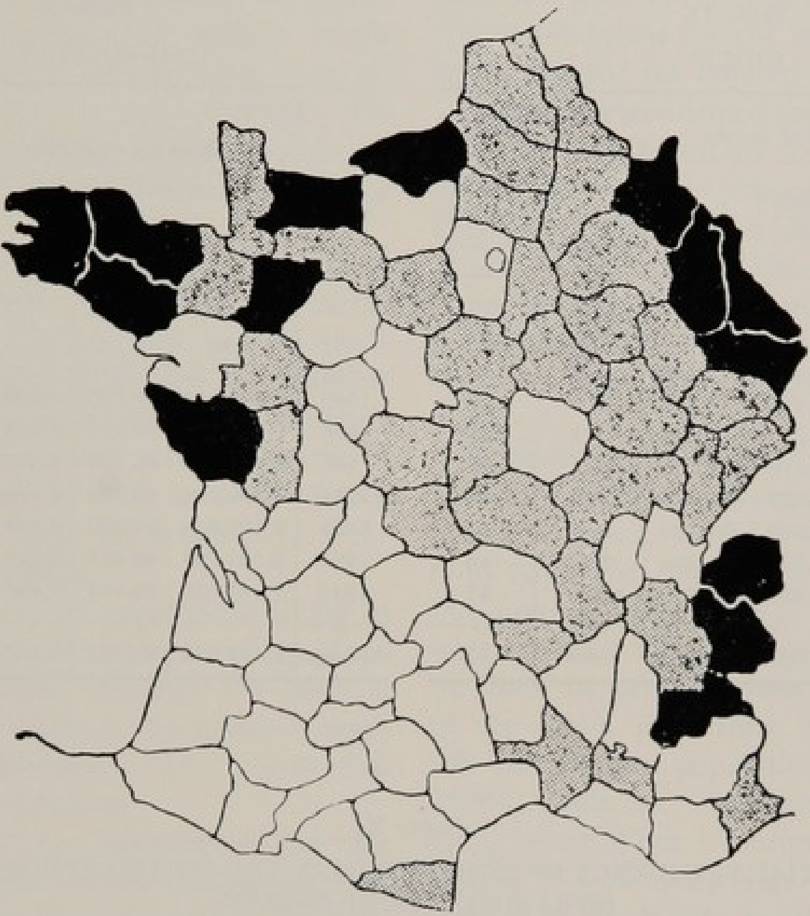


Fig. 38. Distribution of twin births in France (Tourquan).

Table VIII

SPAIN

Year	Number of Births			Multiple Births in Every 1000 Deliveries	Single Births for Every Multiple Delivery
	Single	Multi-ple	Total		
1926	671,430	6,029	677,459	8.8	111
1927	642,823	6,467	649,290	9.9	99
1928	674,709	6,346	681,055	9.2	106
1929	662,380	6,191	668,571	9.2	107
1930	669,851	6,360	676,211	9.4	105
1931	658,943	5,583	664,526	8.4	118
1932	681,349	5,665	687,014	8.2	120
1933	678,640	5,860	684,500	8.6	116
1934	647,492	5,505	652,997	8.4	118
Average	665,290	6,000	671,291	8.9	111

AMERICA

Chile

(See Table IX.)

United States

The frequency of twinning in the United States has been ascertained by Nichols (1907), Greulich (1934), Hamlett (1935), Newman (1940), Arey (1940), Strandskov (1945a, 1945b), Strandskov and Edelen (1946), and Strandskov and Siemens (1946).

United States figures provided by the International Institute of Statistics cover only a period of seven years (Table X). It will be noted that they do not exactly correspond with Strandskov's findings (see Table XI).

Table IX

CHILE[1]

Year	*Number of Births*			*Multiple Births in Every 1000 Deliveries*	*Single Births for Every Multiple Delivery*
	Single	*Multi-ple*	*Total*		
1926	153,518	3,044	156,562	19.4	50
1927	166,162	3,252	169,414	19.2	51
1928	171,305	4,138	175,443	23.6	41
1929	169,571	3,225	172,796	18.7	53
1930	163,320	3,032	166,352	18.2	54
1931	150,304	2,510	152,814	16.4	60
1932	150,634	2,381	153,015	15.6	63
1933	148,326	2,943	151,269	19.5	50
1934	151,438	3,126	154,564	20.2	48
1935	154,459	3,264	157,723	20.7	47
Average	157,903	3,091	160,995	19.0	51

Table X

UNITED STATES

Year	*Number of Births*			*Multi-ple Births in Every 1000 Deliv-eries*	*Single Births for Every Multi-ple Deliv-ery*
	Single	*Multi-ple*	*Total*		
1929	2,201,812	26,759	2,228,571	12.0	83
1930	2,237,311	26,412	2,263,723	11.7	86
1931	2,142,443	25,338	2,167,781	11.7	85
1932	2,101,429	25,349	2,126,778	11.9	83
1933	2,107,571	25,238	2,132,809	11.8	84
1934	2,193,293	26,284	2,219,577	11.8	83
1935	2,181,050	25,464	2,206,514	11.5	86
Average	2,166,414	25,834	2,192,250	11.7	84

Table XI

DIFFERENTIAL FREQUENCY OF TWIN BIRTHS IN THE UNITED STATES—1922-1936 (STRANDSKOV AND EDELEN)

Year	*Total Number of Twin Births*	*Twin Births According to Sex*			*White Twin Births*	*White Twin Births According to Sex*			*Colored Twin Births*	*Colored Twin Births According to Sex*		
		♀♀	♀♂	♂♂		♀♀	♀♂	♂♂		♀♀	♀♂	♂♂
1922	21,163	6,911	7,098	7,154	18,947	6,176	6,304	6,467	2,216	735	794	687
1923	21,444	7,033	7,113	7,298	19,143	6,298	6,298	6,547	2,301	735	815	751
1924	22,751	7,327	7,575	7,849	20,263	6,552	6,659	7,052	2,488	775	916	797
1925	21,531	7,063	6,919	7,549	19,460	6,412	6,173	6,875	2,071	651	746	674
1926	21,739	7,122	7,056	7,561	19,598	6,425	6,309	6,864	2,141	697	747	697
1927	25,752	8,390	8,439	8,923	22,581	7,334	7,357	7,890	3,171	1,056	1,082	1,033
1928	26,786	8,663	8,878	9,245	23,052	7,499	7,555	7,998	3,734	1,164	1,323	1,247
1929	26,489	8,673	8,823	8,993	22,647	7,422	7,504	7,721	3,842	1,251	1,319	1,272
1930	26,128	8,513	8,748	8,867	22,123	7,224	7,316	7,583	4,005	1,289	1,432	1,284
1931	25,067	8,062	8,507	8,498	21,095	6,782	7,074	7,239	3,972	1,280	1,433	1,259
1932	25,081	8,043	8,570	8,468	21,056	6,790	7,102	7,164	4,025	1,253	1,468	1,304
1933	24,990	8,098	8,471	8,421	20,741	6,721	6,926	7,094	4,249	1,377	1,545	1,327
1934	25,993	8,523	8,612	8,858	21,590	7,135	7,054	7,401	4,403	1,388	1,558	1,457
1935	25,197	8,122	8,397	8,678	21,279	6,911	6,983	7,385	3,918	1,211	1,414	1,293
1936	25,569	8,394	8,388	8,787	21,655	7,104	7,059	7,492	3,914	1,290	1,329	1,295
Total....	365,680	118,937	121,594	125,149	315,230	102,785	103,673	108,772	50,450	16,152	17,921	16,377
Average..	24,379	7,929	8,106	8,343	21,015	6,852	6,911	7,251	3,363	1,077	1,195	1,091

Hamlett based his calculations on information gathered from 18 million births chosen at random, which he took from official publications on vital statistics. He made separate studies of the pattern of twinning frequency among white and colored populations.

Out of 16,538,001 deliveries, the white population showed 189,358 multiple births (187,499 twins, 1,829 triplets, and 30 quadruplets). The ratio calculated by Hamlett is one multiple in every 89 single deliveries. This would correspond with the ratio in Prussia, published by Veit in 1855 (1:89), but it is lower than in Belgium (1:55.6) and Norway (1:69.2).

Among the colored populations living in the United States (94% Negroes, 4% Mongols, 2% American Indians) the ratio is 1:69.5. Multiple births in the colored populations have a frequency 25% above that in the white populations.

Hamlett finds no explanation for the rather considerable differences between individual states, such as Kentucky (1:66.8) and Nevada (1:123.7). In the white populations 33% of twins are monozygotic, and slightly less (29%) in the colored groups.

Strandskov, with the assistance of several colleagues, analyzed the twinning phenomenon in the United States with respect to overall frequency, sex ratio, MZ-DZ ratio, frequency of stillbirths, and the like, for the white and colored populations. Strandskov's research material consisted mainly of twin births recorded in the United States over a period of 15 years (1922-1936). We based the data in Table XI on Strandskov's findings. His figures are lower than those reported by the International Institute of Statistics. Strandskov took into consideration only double and no greater multiple births.

Strandskov's twin birth frequencies between 1922 and 1936 correspond to a grand total of 31,487,413 births, and sub-totals of 27,923,410 births for the white, and 3,564,003 births for the colored populations.

Strandskov confirmed the finding that the ratio of twin births to total births is significantly higher in the colored (1.433%) than in the white (1.129%) population. While the sex ratio in the total U.S. population is 48.431% females to 51.569% males, in the twin population, according to Strandskov, it is 49.151% females to 50.849% males.

A report issued in 1947 by the U.S. Public Health Service, covering multiple births over five years (1940-1944), estimated the twin ratios for 100,000 births in the white and colored populations: 1,016.8 for the white; 1,256.6 for the Negro, and 972.2 for the total of other populations. In relation to the white population figure, the ratio for the Negro population is higher by 23.6%, while for other ethnic groups it is 4.4% lower. Thus U.S. figures support the finding of a comparatively higher twin frequency in the Negro population.

Uruguay

Table XII does not include single or multiple births where no child was born alive; a delivery is considered multiple if there are at least two living infants.

Venezuela

Figures reported by the International Institute of Statistics for Venezuela cover only three years, but they merit attention as indicating a very low twinning rate. (See Table XIII.)

OCEANIA AND ASIA

Australia

The figures in Table XIV apply only to deliveries in which at least one child is born alive. Not included are births of aborigine babies.

Table XII

URUGUAY

Year	Number of Births			Multiple Births in Every 1000 Deliveries	Single Births for Every Multiple Delivery
	Single	Multi-ple	Total		
1926	42,166	460	42,626	10.8	92
1927	41,910	464	42,374	11.0	90
1928	44,033	293	44,326	6.6	150
1929	43,311	463	43,774	10.6	94
1930	44,648	535	45,183	11.8	83
1931	43,890	482	44,372	10.9	91
1932	43,260	388	43,648	8.9	111
1933	40,782	434	41,216	10.5	94
1934	40,609	364	40,973	8.9	112
Average	42,733	431	43,165	10.0	101.8

Table XIII

VENEZUELA

Year	Number of Births			Multiple Births in Every 1000 Deliveries	Single Births for Every Multiple Delivery
	Single	Multi-ple	Total		
1927	90,092	323	90,415	3.6	279
1928	92,396	296	90,692	3.2	312
1929	92,347	317	92,664	3.4	291
Average	91,611	312	91,923	3.4	294

Japan

Hamlett indicated a very low frequency in Japan, equal to 1:301. Census figures for Japan show the occurrence of only one multiple delivery in every 299.5 single births (Komai and Fukuoka).

Oku (1933) suggested as an explanation that in some Japanese circles there is a tendency to believe that a twin birth brings bad luck. It is therefore an undesirable event and should be kept secret. According to the author, this explains why the census records show a frequency of 4.37 per 1,000, while the maternity hospitals give a frequency of 6.78 per 1,000.

With a theoretical correction, Oku considered the true frequency to be 7.2 in every 1,000 births. 58 per cent of twin births would be MZ twins and 42 per cent DZ. The density of population has no influence on the percentage of twin births. In the colder regions the total number of

Table XIV

AUSTRALIA

Year	Number of Births			Multiple Births in Every 1000 Deliveries	Single Births for Every Multiple Delivery
	Single	Multi-ple	Total		
1926	130,333	1,423	131,756	10.8	92
1927	130,754	1,472	132,226	11.1	89
1928	131,353	1,423	132,776	10.7	92
1929	126,859	1,320	128,179	10.3	96
1930	125,530	1,439	126,969	11.3	87
1931	115,987	1,271	117,258	10.8	91
1932	108,742	1,107	109,849	10.1	98
1933	108,983	1,154	110,137	10.5	94
1934	107,158	1,171	108,329	10.8	92
1935	109,092	1,157	110,249	10.5	94
Average	119,479	1,293	120,772	10.6	92

Table XV

JAPAN

Year	Number of Births			Multiple Births in Every 1000 Deliveries	Single Births for Every Multiple Delivery
	Single	Multi-ple	Total		
1929	2,179,066	7,437	2,186,503	3.4	294
1930	2,187,064	7,846	2,194,910	3.6	280
1931	2,203,282	7,971	2,211,253	3.6	276
1932	2,285,334	8,452	2,293,786	3.7	270
1933	2,219,911	7,707	2,227,618	3.5	288
1934	2,140,887	7,934	2,148,821	3.7	270
1935	2,288,202	8,996	2,297,198	3.9	254
Average	2,214,820	8,049	2,222,869	3.6	276

births, including twin births, is generally higher than in warmer localities.

Based on the number of births reported by Japanese hospitals between 1904 and 1931, Komai and Fukuoka (1936) found a frequency of 1:92.43, i.e., 1,520 multiple births in 140,508 births chosen at random. The same authors found a ratio of 1:74.1, i.e., 97 multiple births in 7,191 births chosen at random in Korea. Census figures obtained in large cities gave the following distribution of the sexes: 6,258 ♂♂ twins; 1,510 ♂♀ twins; and 5,488 ♀♀ twins. According to Komai and Fukuoka, DZ twins are relatively less frequent in Japan than in Europe.

Bearing in mind the uncertainties indicated by the authors, it is interesting to see the figures drawn up for Japan by the International Institute of Statistics (see Table XV). According to Fisher, multiple births would be extremely rare in Annam and Cochin-China, where it seems one twin birth occurs only in about 10,000 deliveries. Also, Chiarugi observed that twins seem to be almost unknown in certain provinces of China. The possibility that many twins are kept secret, as in Japan, may have to be taken into account.

2. FREQUENCY RATIO BETWEEN QUANTITATIVELY DIFFERENT TWIN BIRTHS: HELLIN'S LAW

Figures on the frequency of the twinning phenomenon may be also analyzed according to the number of infants produced by multiple births. The total number of single births may then be compared with twin births, with triplet births, with quadruplet births, etc. in order to determine the ratio between *quantitatively* different multiple births.

By analyzing Müller's statistical findings on births occurring in Prussia between 1826 and 1849 (13,360,557 births), Veit, in 1855, calculated that double births were in a ratio of 1:89 of the total number of births; triple births $1{:}89^2$ and quadruplet births $1{:}71.3^3$.

In 17.7 million births, Sicklet (1859) found one pair of twins in every 83 deliveries, one set of triplets in every 8,007 births, and one set of quadruplets in every 385,499 births.

In 1859, analyzing the total of 19,698,322 births in Central Europe, Waeppaus found 226,807 double and 1,623 triple births, which correspond respectively to the ratio 1:89 and $1{:}89^2$. In 1877, Neefe, out of 50 million births, worked out a ratio of 1:82.7 for double, $1{:}82^2$ for triplet, and $1{:}82.4^3$ for quadruplet births.

In 1892, v. Prinzing studied 63 million births in Germany from 1871 to 1880. He calculated that the ratio for double births was 1:85.6; for triplet births $1{:}84^2$ (one set of triplets in about 7,000 births); for quadruplet births $1{:}92^3$ (one set of quadruplets in about 780,000 births).

It is apparent that even as far back as Veit's investigations in 1855, the frequency of triplet and quadruplet births was distributed in a distinct and constant ratio which lent itself to statistical calculation.

Hellin devised the best formula to express the mutual frequency ratio between the various degrees of multiple births. Gaining wide recognition, the formula became known as Hellin's Law. In 1895 Hellin wrote: "The greater the number of twins born at the same time, the lower the frequency, which diminishes proportionately. While one can say that in the human species an average number of one twin birth is found in every 89 single births, one triplet birth in every 89^2 single births, and one quadruplet in every 89^3, generally, within the limits of probability, one x multiple birth would be seen in every $89^{(x-1)}$ single births." Subsequent studies gave ample support to Hellin's Law. In 1901, Ruppin examined births occuring in Prussia between 1890 and 1899, averaging 1,202,570 yearly. Among these, the frequency of twin births was 1:80, while that of triplet births was $1:86.6^2$.

On the basis of over 50 million births, Guzzoni in 1900 found a ratio of 1:87 for twin and $1:84.3^2$ for triplet births. In 1920, Stöckel established the frequency of 1:80-90 for twin births, noting that in order to obtain a closer agreement with the statistical values, a correction could be made, extending from slightly under 80 to slightly over 90.

Dahlberg, who in 1926 diligently reviewed the bibliography on the question, concluded that it may be assumed that multiple births follow Hellin's Law, according to which twin births occur in every $\frac{1}{n}$ single births, triplet births in $\frac{1}{n^2}$, quadruplet births in $\frac{1}{n^3}$, quintuplet births in $\frac{1}{n^4}$, where n varies from a little less than 80 to a little more than 90.

Analyzing approximately 100 million births, Livi (1922) established a statistical law of his own on the distribution of multiple births. This law considered a progression based on the ratio of 1:84.25. Working on some 300 million births, Patellani (1923) discovered that, as compared with the ratio of quadruplet births to triplets, the ratio of quintuplets to quadruplets was clearly higher (ratio of twin births to single ones, 1:84; triple births to twins, 1:89; quadruplet births to triplets, 1:84; quintuplet births to quadruplets, 1:43).

Applying the ratios indicated by Hellin's Law to the figures shown for the phenomenon of twinning in Italy, results are obtained which do not quite correspond with previous estimates. Applying Hellin's Law to the data found in the statistics on twin births in Italy over a period of 5 years,

Table XVI

Year	*Ratio Between Twin and Single Births*	*Ratio Between Triplet and Single Births*
1931	1:73.871	$1:6503.930 = 1:80.647^2$
1932	1:74.475	$1:6320.088 = 1:79.499^2$
1933	1:71.676	$1:6775.810 = 1:82.316^2$
1934	1:74.942	$1:5682.460 = 1:75.382^2$
1935	1:73.188	$1:6346.069 = 1:79.662^2$

from 1931 to 1935, Gedda obtained the results presented in Table XVI.

Findings obtained by Gedda and others in checking the validity of Hellin's Law would seem to suggest that it is perhaps more a principle than a law. The principle indicates that the various degrees of multiple births do not occur at random and their occurrence is regulated by population constants which probably find different mathematical expression according to the interaction of hereditary and environmental factors.

Therefore, we find ourselves in agreement with the opinion expressed in the U. S. Public Health Service's survey of multiple births (1947) which referred to Hellin's Law as "a rough rule of thumb." A number of authors—Zeleny, 1921; Gini, 1923; Jenkins, 1927; Fisher, 1928; Greulich, 1930; Hamlett, 1936; Jenkins and Gwin, 1940; and Strandskov, 1945—have pointed out that Hellin's Law ought to be reconsidered for the different types of zygosity, for problems of intrauterine survival, as well as those of multiple-birth registration.

3. FREQUENCY RATIO BETWEEN QUALITATIVELY DIFFERENT TWINS: MONOZYGOTIC AND DIZYGOTIC (WEINBERG'S DIFFERENTIAL METHOD)

Figures on the frequency of twin births may be dealt with in still another way, according to the type of twins—whether similar, i.e., monozygotic, or dissimilar, i.e., dizygotic. Investigations of this kind were undertaken as soon as twins became the subject of biological studies in the second half of the Nineteenth Century. However, the results were contradictory, leaving this important problem unsolved for a long time.

While prevailing medical opinion clung to erroneous findings which tended to indicate that the frequency of monozygotic twins was as low as 12 to 15% of all twin births, the correct figures were obtained by mathematical calculation as early as 1902. Here we have an excellent example of how calculations may anticipate the conclusions eventually reached by science and verified by experiment.

On the basis of his research on sex distribution, Bertillon in 1894 had come forward with the hypothesis that out of the total number of twins, it was possible to determine the percentage of MZ twins by mathematical calculation. He estimated a percentage of MZ twins corresponding to 30 per cent of all twin pairs, but since experimental findings at that time showed significantly lower percentages, the author abandoned his studies in this field.

Hensen, too, after a similar study in 1881 had found that by basing calculations on the statistical findings of sex distribution one could reach the "impossible" figure of 26 per cent for MZ twins.

Weinberg, in two publications (1902) and a series of scientific discussions, presented his differential method. This technique makes it possible to calculate mathematically the percentage of MZ twins from the number of pairs of opposite sex.

Weinberg's method, previously outlined by Bertillon and Hensen, was expressed in the following formula: "As each egg is independently fertilized, the sex of its germ is also determined separately: thus twins of the same or of opposite sex may occur. According to the laws of probability, equal numbers of same-sexed and of opposite-sexed pairs may occur."

Lotze, applying Weinberg's method to experimental data, came to the following conclusions: "As 106 male births occur for every 100 female births, the probability for single births is 0.514 for a male birth and 0.486 for a female. The probability that opposite-sexed pairs may occur among biovular twins is therefore $2 \times 0.514 \times 0.486 = 0.4996$. Half of all DZ cases should therefore be opposite-sexed pairs."

However, Weinberg maintained that the slight majority of males over females could be discounted and for practical purposes it was not necessary to take into consideration the difference in frequency of the two sexes. Thus it follows that there is an equal probability of the occurrence of pairs of twins either of the same or of opposite sex among DZ twins. Therefore, by doubling the values referring to twin pairs of opposite sex, which are certainly DZ, it is possible to determine the total values of all DZ pairs, including those of the same sex. Then, by subtracting these total figures from those referring to all twin pairs, the number of MZ pairs may be obtained.

In other words, if the number of births of opposite-sexed twins in a given year and place, or the number of infants produced by such births, is multipled by two, then the total number of DZ births or infants produced from DZ deliveries will be known. However, since the calculation is only an approximation, it is preferable to rely on percentages rather than absolute figures. Thus, if the percentage representing pairs of opposite sex is doubled, the result is the percentage of all DZ pairs. Subtracting this figure from 100 (representing the total number of twin births), the result is the percentage of MZ pairs.

For example, according to Prussian statistics between 1826 and 1896, births of opposite-sexed twins amounted to 37.3% of the total number of twin births. With Weinberg's method, the percentage of all DZ pregnancies is therefore 37.2×2=74.6% and the frequency of MZ twins 25.4%.

Applying his differential method to twin birth statistics of various countries, Weinberg obtained percentages of MZ pairs varying from 33.4 to 21%. Such figures agreed well enough with the experimental findings Weinberg had obtained from a clinical sampling of 839 cases of known zygosity in the literature where he estimated the percentage of MZ pairs as 21.2%. After defending his method in a discussion with Ahlfeld in 1903, Weinberg lowered the percentage of MZ pairs found in this material to 20.9%.

Prinzing, in 1908, departed from Weinberg's method by first establishing the percentage of genuine MZ twins, as compared with that of DZ pairs (same-sexed pairs with evidence of a double chorion, plus the opposite-sexed pairs). The remaining pairs (same-sexed pairs lacking recorded evidence of a double chorion) were distributed according to the ratio of authentic MZ to authentic DZ same-sexed pairs. Thus the percentage of genuine MZ pairs (19.6%) was raised to 26.3% assumed MZ pairs. It should be noted that Weinberg's method gave a percentage of 26.2 MZ pairs for the same material.

In 1914, Mayer in turn also deviated from Weinberg's method, carrying out his calculations along the same lines as Prinzing. Mayer divided the number of twin pairs of unknown zygosity equally between the groups of known MZ and known DZ twins. In this way he reached a percentage of MZ twins equal to 21.8, while the differential method gave a percentage of 20.1 on the same material.

As may be seen, the variations introduced by both Prinzing and Mayer do not substantially contradict the simpler method proposed by Weinberg. The principle which inspired the differential method was later used independently of Weinberg by Cobb in 1915 and applied to material from the state of Connecticut.

Weinberg's method was authoritatively brought to the attention of all students of geminology by Dahlberg who wrote in a well-known monograph (1926) that Weinberg's excellent work of 1902 had not received the attention it deserved. According to Dahlberg, it should be especially noted that Weinberg's differential law is of fundamental importance when distinguishing between MZ's and DZ's, and the results obtained by this method prove, in agreement with the most reliable experimental findings, that monozygotic twin births are nearly 20-30% of total twin births, and 0.30-0.40% of the total number of births, while dizygotic twin births are 0.70-1% (or slightly more) of the total number of births.

The frequencies of MZ twins estimated in this manner ranged from 20 to 30%. For European countries, Orel obtained values between 23 and 25%. Since the frequency of MZ twins in Germany corresponds to 25.4% of all twin births, it would be 3 to 3.5‰ of all births, and therefore the birth of MZ twins in Germany would occur approximately once in every 340 single births.

In 1934 Weinberg checked his method on a sampling of 1,112 twin births, and obtained an empirical number of DZ twin births, higher than that which calculation would have led him to suppose. He proposed a formula for correcting the average error of this calculation.

Later, Schultz (1936), v. Verschuer (1940) and several other authors also supported Weinberg's method. However, in 1940, v. Schelling pointed out that this method of estimating MZ twins was not completely reliable, and he therefore proposed suitable corrective formulas.

Since twinning statistics provide only the number of opposite-sexed twin pairs v and the number of same-sexed pairs g, the number of uniovular pairs e is obtained by the differential method as follows:

$$e = g - v$$

v. Schelling suggested the use of the following formula:

$$\frac{100\,v}{v+g} \pm \frac{300}{v+g}\sqrt{\frac{vg}{v+g}} \qquad (1)$$

With the choice of the + or the − sign in formula (1), two values are obtained, v' and v'', so that the various percentages of v (DZ of opposite sex) are found in 99.73% of cases between v' and v'', i.e., $v' < v < v''$.

In regard to e, the author gave the limitation (2) and the formula (3):

$$100 - 2v'' < e < 100 - 2v' \qquad (2)$$
$$e = g - v \pm \sqrt{2v} \qquad (3)$$

In this way, v. Schelling was able to complete an analysis, for example, of the figures on twin births in Germany in 1933. Since $v = 4{,}129$ and $g = 7{,}529$, according to formulas (1) and (2), we have:

$$34.09\% < v < 36.75\%$$
$$26.51\% < e < 31.82\%$$

and from this, according to formula (3):

$$e = 3{,}400 \pm 90.897$$

For the complete series of MZ twins, v. Schelling arrived at the following results:

$$20.2\% < e < 72.8\%$$

The work of Strandskov and Edelen in the United States showed that the frequency of MZ twins in the white population differs from that in colored populations. The frequency of MZ and DZ births is calculated according to Weinberg's differential method, taking into account the proportion of the sexes in the whole population and the twin population, and the theoretical ratio between the two sexes (50:50). The results calculated from these three angles agree very well and show the frequency of MZ twins as being 33.46% of the total twin population, 34.17% of the white twin population, and 28.89% of the colored twin population.

Comparing the percentages of MZ and DZ pregnancies in the white and colored population, and their relation to the total number of births in the U.S.A., Strandskov and Edelen obtained the results shown in Table XVII. From these figures it may be deduced that the higher frequency of twinning in colored populations is associated with higher values of MZ and DZ twins. Strandskov and Edelen maintain that both exogenous and inherited endogenous fac-

Table XVII

DIFFERENTIAL FREQUENCY OF TWIN BIRTHS IN WHITE AND COLORED POPULATIONS (WEINBERG'S METHOD)

	All Single and Multiple Births	*MZ Births*		*DZ Births*	
		Total	*%*	*Total*	*%*
Total	31,487,413	122,253	0.388	243,427	0.773
White	27,923,410	107,669	0.386	207,561	0.743
Colored	3,564,003	14,584	0.409	35,866	1.006

tors are responsible for these differences.

In regard to Italy, Gedda and Cherubini calculated the frequency of MZ and DZ twin births, according to Weinberg's method, in each individual year and in the totals of the five-year period between 1931 and 1935, as may be seen in Table XVIII. It will be noted that *the frequency of MZ twin births in Italy during the years 1931 through 1935 corresponds to 29.2%*.

Furthermore, Gedda and Cherubini made similar calculations on figures of twin births occurring in Rome over a period of eight years (1938 to 1945).

As may be seen in Table XIX, the percentage of MZ twins calculated from the total number of twin births in Rome is 32.93 and that of DZ pairs 67.07. By comparing these results with those obtained on the total number of twins born in Italy, it would seem that the qualitative differences in twinning are also subject to geographical conditions.

Table XVIII

DIFFERENTIAL FREQUENCY OF TWIN BIRTHS IN ITALY WEINBERG METHOD (1931-1935)

Year	*Total*	*Of Opposite Sex*	*MZ*		*DZ*	
			Total	*%*	*Tot l*	*%*
1931	13,999	5,007	3,985	28.5	10,014	71.5
1932	13,408	4,702	4,004	29.9	9,404	70.1
1933	13,991	4,979	4,033	28.8	9,958	71.2
1934	13,345	4,660	4,025	30.2	9,320	69.8
1935	13,700	4,870	3,960	28.9	9,740	71.1
Avg.	13,688	4,843	4,001	29.2	9,687	70.8

Table XIX

DIFFERENTIAL FREQUENCY OF TWIN BIRTHS IN THE CITY OF ROME WEINBERG METHOD 1938-1945

Year	*Total*	*Of Opposite Sex*	*MZ*		*DZ*	
			Total	*%*	*Total*	*%*
1938	389	130	129	33.16	260	66.84
1939	389	136	117	30.07	272	69.92
1940	368	130	108	29.35	260	70.65
1941	334	118	98	29.34	236	70.66
1942	339	105	129	38.05	210	61.95
1943	297	101	95	31.99	202	68.01
1944	267	90	87	32.58	180	67.42
1945	289	86	117	40.48	172	59.52
Total. . .	2,672	896	880	32.93	1,792	67.07

Chapter V

ETIOLOGIC BACKGROUND FACTORS IN TWINNING

HAVING DISCUSSED statistical aspects of the twinning phenomenon, we may now consider its possible causes. What are the factors that determine multiparity? Statistical studies have helped to establish the fact that the frequency of twinning varies from one country to another, and that geographical variations do not affect monozygotic and dizygotic twinning to the same extent, having a more pronounced influence on the latter.

Geographical variability may be explained on three counts: (1) Environmental components, such as climate and food, may influence multiparity. (2) Ethnic factors may alter the tendency of members of different populations to have twins. (3) A combination of these two factors may be at work.

The mathematical ratio between the different degrees of multiparity, as expressed in Hellin's Law, shows that the twinning phenomenon, though unusual in the generally uniparous human species, does follow a quantitative rhythm which recurs everywhere. Therefore it is not an accidental phenomenon, but is determined by certain laws regulating generation in the human species.

EARLY ETIOLOGIC THEORIES

Hypotheses found in the early literature on twins include those on atavism, degeneration and intoxication. Interest in twins and their biological significance became fashionable with scientists when attention was being focused on evolutional phenomena. Far from regarding twins as a means of making objective observations (experimental method), however, this early interest represented a trend toward biological thinking, guided by the theories of Darwin, Lamarck and Haeckel.

This atmosphere paved the way for a transformist theory of the twinning phenomenon. According to it, multiparity was an ancestral carry-over, not yet eliminated from the human species—a "transitory reversion" (Patellani) attesting to the derivation of the normally uniparous human species from lower multiparous species. This hypothesis of atavism was used in connection with other somatic peculiarities of the human organism, and was predominant for some time in the literature on twins.

Closer to the current concept of mutation is the hypothesis that regarded multiparity as a degeneration—inasmuch as mutations are usually considered minus variants with respect to the qualities of the species. Some authors even claimed a higher frequency of twinning in mentally defective families (also attributed for a while to a degeneration process), but neither hypothesis rested on sufficient scientific evidence.

Larger (1901) suggested such causes as epilepsy, syphilis, alcoholism and tuberculosis when studying the twinning phenomenon in the families of the Caesars, the Carolingians, and the Bourbons, having also been impressed by the degeneration theory. Even Lenz (1923) was inclined to believe that some external causes, chiefly alcoholism,

Table XX

ITALIAN LIVE BIRTHS 1935-1937, ACCORDING TO MATERNAL AGE

Age	*Year*				*Fertility Index*
	1935	1936	1937	1935–1937	
12	—	2	—	2	—
13	9	9	15	33	0.13
14	120	118	123	361	0.32
15	713	796	802	2,311	1.87
16	1,488	2,588	2,922	6,998	6.96
17	3,596	4,001	6,549	14,146	16.09
18	7,971	6,943	7,638	22,552	29.99
19	16,493	12,475	11,897	40,865	48.59
20	28,622	23,482	19,499	71,603	70.83
21	37,654	34,799	33,456	105,919	94.37
22	49,581	43,766	47,040	140,387	117.16
23	54,497	52,934	55,896	163,327	136.60
24	60,793	55,301	62,679	178,773	151.01
25	63,381	59,692	62,413	185,486	159,97
26	62,295	60,497	64,257	187,049	164.55
27	60,160	61,169	63,161	134,490	164.84
28	56,590	56,843	60,930	174,363	162.09
29	52,891	53,083	56,002	161,996	157.31
30	52,331	51,171	51,935	155,437	152.16
31	44,303	47,822	48,800	140,925	145.23
32	43,891	43,372	45,844	133,107	137.97
33	38,598	40,119	41,134	119,851	131.04
34	39,799	37,055	38,266	115,120	125.82
35	38,755	35,090	34,544	108,389	119.52
36	32,627	33,828	32,057	98,512	111.55
37	30,419	29,312	30,138	89,876	102.07
38	27,705	26,971	25,973	80,649	92.55
39	23,121	23,677	23,289	70,087	82.07
40	20,669	19,595	19,478	59,742	70.37
41	14,905	15,578	15,244	45,727	57.39
42	12,577	11,743	11,509	35,829	57.39
43	8,522	8,204	7,968	24,694	31.68
44	5,515	5,006	5,051	15,572	20.56
45	3,081	2,903	2,747	8,731	11.80
46	1,613	1,529	1,402	4,544	6.13
47	724	663	669	2,056	2.82
48	353	236	316	905	1.21
49	150	132	121	403	0.50
50	68	59	29	156	0.23
51	25	35	14	74	0.12
52	29	33	9	71	0.09
53	18	10	5	33	0.05
54	12	10	5	27	0.04
55+	—	5	—	5	

might interact with hereditary factors in determining the twinning phenomenon.

The rather vague hypothesis of degeneration gradually developed into that of intoxication, upheld especially by French authors. Here multiparity was ascribed to exogenous damage sustained by either the gametes or the embryo. In the latter instance, the embryonic pathology was seen in a condition known as blastophthoria.

On this basis the hypothesis of intoxication was but one step removed from that of syphilitic infection as the presumed cause of degeneration. Despite many doubts as to the syphilitic etiology of multiparity (Fournier in 1898, Puech in 1909, Apert in 1923), Pointin (1908) found 5 cases of syphilis in 27 twin pregnancies; Popoff (1908) 8 cases of syphilis in 38 twin pregnancies.

The symptoms described included abortions, premature birth, hydramnios, hydrocephalus, and the like. Massoni (1912) found 1 case with a positive Wasserman reaction in 13 twin pregnancies. Grancher also suspected a familial (congenital) syphilis because of the observed association of hydramnios and twin births. Marfan believed twinning occurred more often in marriages of syphilitics; Hutinel, Bar, Couvelaire and others thought remote ancestors, rather than the twins' parents, might have been syphilitic.

De Blasi (1911), dealing with syphilis and pregnancies, reported the case of a syphilitic man whose wife, in 5½ years, had nine miscarriages with a total of 12 fetuses, including one set of twins and one of triplets.

Merkeln and Devaux (1921) also reported on the connection between twinning and syphilis.

MATERNAL FACTORS

The principal maternal factors studied have been the physical characteristics, age, menstruation and fertility. Hellin believed that women of slight build are more apt than others to conceive twins, and maintained that the ovaries of mothers of dissimilar twins probably contained a greater number of follicles.

Puech was of the opinion that multiparity might be related to large ovaries. Both these opinions were assumptions based on studies of comparative anatomy and, like the older theories of Hellin, were not upheld by adequate evidence. The same weakness applies to the theory of Williams ascribing the phenomenon to functional overactivity of the ovaries.

Clerico (1904), in a study of 50 mothers of twins, reported that twin frequency increases with the extension of the mother's pelvic diameter. In the narrow pelvis group he found a frequency of 0.51%; in the medium pelvis group 1.64%, and in the wide pelvis group 3.91%.

According to Dahlberg, however, these findings may be correlated with maternal age and thus have no specific significance.

Another maternal characteristic which may be considered on a more solid basis falls under the heading of what Chiarugi termed Duncan's Law. It may be expressed as follows: *The number of multiple births increases with the number of pregnancies and the age of the mother.*

The relationship with maternal age has some curious aspects. If the probability of twin pregnancies followed that of single ones, the curve showing distribution of twin births would likewise be bell-shaped, with the lowest frequencies at the beginning and end of the fertile period, and the high point between 20 and 30 years of age. This average maternal age for single pregnancies—i.e. the maternal age during which the greatest number of single births occurs—is important for purposes of comparison with the average age of mothers of twins.

Statistical findings show that the average

Table XXI

COMPARATIVE RATES OF TWIN BIRTHS ACCORDING TO ZYGOSITY AND MATERNAL AGES, EXPRESSED AS PERCENTAGES OF TOTAL NUMBER OF BIRTHS (WEINBERG'S DIFFERENTIAL METHOD*)

	Maternal Age							*Total*[2]
	15-20	20-25	25-30	30-35	35-40	40-45	45-50	
Denmark 1896—1910								
Twin births of opposite sex	67	675	1,374	1,519	1,379	472	10	5,498
% MZ	0.42	0.36	0.35	0.41	0.47	0.40	0.31	0.38
% DZ	0.36	0.57	0.87	1.18	1.57	1.25	0.30	0.99
France 1902—1906								
Twin births of opposite sex	539[1]	2,494	4,298	4,153	3,166	991	122	16,069
% MZ	0.34	0.27	0.31	0.33	0.34	0.32	0.21	0.32
% DZ	0.47	0.46	0.69	0.97	1.20	0.94	0.84	0.76
France 1907—1910								
Twin births of opposite sex	217	1,964	3,396	3,504	2,774	804	23	12,818
% MZ	0.31	0.31	0.34	0.38	0.38	0.36	0.35	0.34
% DZ	0.25	0.45	0.73	1.06	1.44	1.12	0.34	0.80

*From Dahlberg, modified.

[1]Including twins born to mothers under 15 years of age.

[2]Including twins born to mothers of unknown age.

age of Italian mothers for single births lies between the twenty-fourth and thirtieth year. Regarding twin births (from 1866), Duncan showed that the average maternal age (established, according to English statistics, between the thirty-fifth and thirty-ninth years of age) does not correspond with that found in single births. Duncan's observations have been criticized because while he based his figures for single births on unselected material from the cities of Glasgow and Edinburgh, he used only clinic cases (and hence less representative material) for his study of twins. Nevertheless, Duncan is to be credited with having noted the difference.

In a Danish survey (1882), Ditzel had found an average maternal age of 35 to 39 years. Some years later (1891), in a study of 677 twin births out of a total of 44,294 births recorded in Copenhagen, Lauritzen confirmed an average maternal age of 35 to 39 years. Further, according to statistics obtained in what was then St. Petersburg, Munich and New South Wales (1898), Bertillon estimated that twin frequencies were highest when the mothers were between 35 and 40 years old.

Studying Finnish (1881-1890) and Saxon (1881-1885), as well as Danish, French and Hungarian statistics, Weinberg noted the greatest twin frequency at about the fortieth year of the mother's age. He also observed that the increase in twin births, paralleling that of maternal age, was limited largely to DZ twins, while the frequency of MZ births seemed to remain constant (Table XXI). Rumpe (1891) noted a comparative consistency in the rates of MZ twins, and Rabinowitsch in 1913 found slight mean maternal age differences between similar and dissimilar twins.

Other authors also studied this problem in the two zygosity groups. According to Prinzing (1908), DZ twins are appreciably increased in proportion to the age of the mothers, while MZ's show only a very slight increase. In Apert's study (1913), the maximum frequency of twins was found when the mother was between 30 and 39 years of age. The data of Wedervang (1924) also agreed with those of Weinberg.

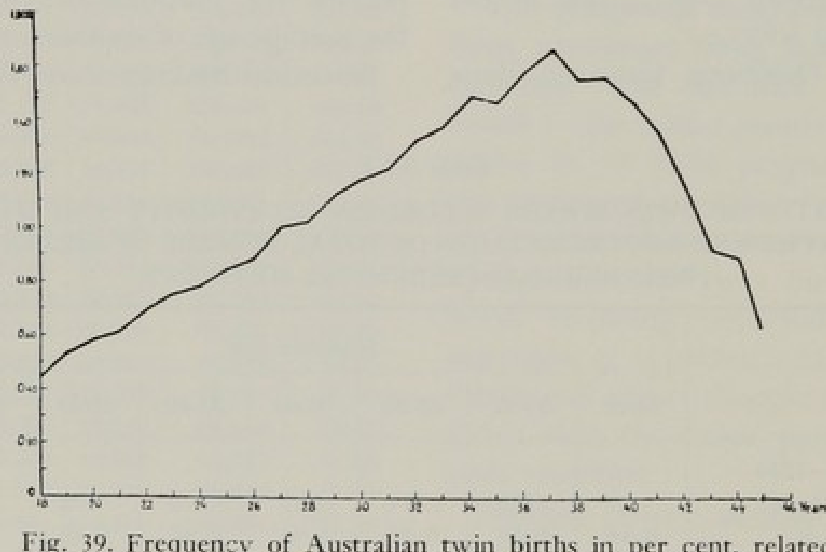


Fig. 39. Frequency of Australian twin births in per cent, related to maternal age (1908-1923; Czuber).

The quantitative increase in twin births with increasing maternal age was also confirmed by Czuber (1923) on the basis of Australian birth statistics (1908-1923) which were particularly impressive because the investigator subdivided his figures into yearly groups. In this way, he was able to establish that the maximum twin frequency (1.67%) in Australia occurred at the mother's thirty-seventh year of age (Fig. 39).

As shown in this graph, it is not quite accurate to state that the number of twin births increases with the age of the mother; it does increase with the age of the mother until it reaches a maximum and then it declines. For instance, in Australia, up to the thirty-seventh year the increase in years and in multiple births is consistent. From then on, as the age increases the number of twin births apparently decreases.

What actually happens is a forward shift of the average age of mothers of twins, as compared to that of mothers of single children. Such a shift is clearly shown in Lotze's graphically arranged data (Fig. 40), and, as mentioned before, refers chiefly to DZ twins. The ratio of MZ twins to the total number of births remains essentially unchanged.

The frequency of twin births was later reconsidered by Weinberg (1933), and also by Yerushalmy (1940). The latter studied multiple births taken from a total of some 11 million deliveries in the United States, with respect to the relationship between multiparity and maternal age. The frequency of DZ twins in this study increased with the age of the mother, while that of MZ twins decreased. The father's age was shown to be of no importance in this connection. Corroborative results were obtained by Enders and Stern (1948).

A similar study of the influence of maternal age on Italian twin statistics was conducted by the author on the basis of data provided by the Italian Institute of Statistics (1930-1937). The results are shown in Table XXII, with the rates of single, twin and triplet pregnancies recorded for seven maternal age groups, and the highest frequency in each group set in heavy print.

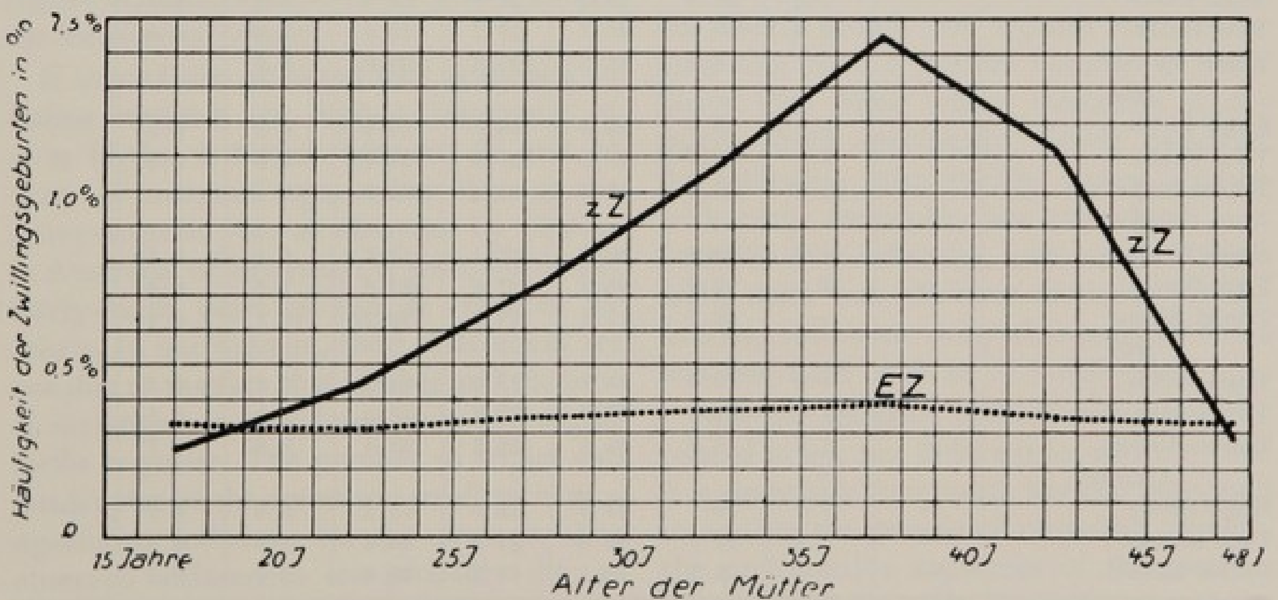


Fig. 40. Zygosity distribution according to maternal age (Lotze).
(Häufigkeit der Zwillingsgeburten in %=Frequency of twin births in %.
Jahre=years. Alter der Mutter=Age of the mother (in years). EZ=MZ. ZZ=DZ.)

It will be noted that Duncan's finding that the frequency of multiparity increases

Table XXII

ITALIAN BIRTH RATES, ACCORDING TO MATERNAL AGE

(1930-1937)

Types of Birth	*Maternal Age*								
	-15	15-20	21-24	25-29	30-34	35-39	40-44	45-49	50-
1930									
Single Births	..	5.7	19.6	**28.0**	23.4	15.8	6.7	0.8	..
Twin Births	..	2.5	12.3	24.9	**28.8**	23.3	7.8	0.4	..
Triplet Births*	—	1.2	9.0	25.7	**32.9**	21.6	9.6	—	—
1931									
Single Births	..	6.0	20.0	**28.1**	23.0	15.5	6.7	0.7	..
Twin Births	..	2.9	12.4	24.9	**28.3**	23.1	8.0	0.7	..
Triplet Births*	—	2.6	7.1	20.6	29.7	**32.3**	7.7	—	—
1932									
Single Births	..	5.7	20.0	**28.5**	22.9	15.6	6.6	0.7	..
Twin Births	—	2.7	12.6	25.5	**27.6**	23.5	7.8	0.3	..
Triplet Births*	—	1.2	9.5	17.1	28.5	**34.2**	9.5	—	—
1933									
Single Births	..	5.5	19.8	**28.9**	22.7	15.6	6.8	0.7	..
Twin Births	—	2.8	12.8	24.6	**27.0**	24.2	8.1	0.5	..
Triplet Births*	—	1.4	6.7	13.4	30.9	**36.9**	10.7	—	—
1934									
Single Births	..	5.4	19.9	**29.2**	22.7	15.4	6.7	0.7	..
Twin Births	..	2.4	13.1	25.1	**27.7**	23.4	7.9	0.4	..
Triplet Births*	—	1.7	6.4	22.5	26.6	**33.0**	9.8	—	—
1935									
Single Births	..	5.2	19.9	**30.0**	22.3	15.5	6.5	0.6	..
Twin Births	—	2.5	12.3	26.5	**26.5**	24.1	7.8	0.3	..
Triplet Births*	—	1.3	10.5	19.6	24.2	**33.3**	11.1	—	—
1936									
Single Births	..	4.6	19.0	**30.6**	23.1	15.7	6.4	0.6	..
Twin Births	—	2.1	12.4	26.3	**27.6**	23.3	7.9	0.4	..
Triplet Births*	—	—	12.7	17.4	28.9	**30.2**	10.1	0.7	—
1937									
Single Births	..	4.4	19.8	**31.2**	23.0	14.9	6.2	0.5	..
Twin Births	—	2.1	12.6	27.6	**27.7**	22.5	7.2	0.3	..
Triplet Births*	—	1.3	15.9	24.5	**25.8**	23.2	8.6	0.7	—
Average									
Single Births	—	5.3	19.7	**29.3**	22.9	15.5	6.6	0.7	—
Twin Births	—	2.5	12.5	25.6	**27.7**	23.4	7.8	0.4	—
Triplet Births*	—	1.4	9.7	20.1	28.3	**30.6**	9.7	0.2	—

*Including quadruplets and, in 1933, one set of quintuplets.

with maternal age was confirmed with respect to both twin and triplet births, as against single births. Moreover, since the frequencies of twin and triplet births were considered separately, it was possible to show that the highest frequencies of these births do not generally occur in the same maternal age groups.

While the greatest frequency of single births always coincides with the maternal age of 25 to 29 years, that of twin births occurs at the age level of 32 to 35 years of age, and that of triplets (six times out of eight) at 35 to 39 years. In other words, it is the number of fetuses, rather than multiparity as such, that shifts the peak toward higher maternal age in a manner directly proportional to that number; i.e. the shift increases with the increase in the number of fetuses.

This observation holds true for each year from 1931 through 1936, as well as for the total period of eight years from 1930 to 1937, but not for the years 1930 and 1937. It may be stated, therefore, that the number of fetuses induces an increase in direct proportion to the mother's age. In other words, Duncan's theory that multiparity increases with the mother's age is supplemented by the role played by the number of fetuses. This principle may be formulated as follows: *The higher frequency of births in the human species becomes shifted towards higher maternal ages in direct proportion to the number of fetuses.*

It should also be noted that according to Italian statistics the highest frequency of twin births is found between 30 and 34 years of maternal age, rather than at the thirty-seventh year as observed by Czuber in Australia, or between the thirty-fifth and thirty-ninth years of age, as reported by others. In our opinion, these differences are not due to the fact that Czuber and the other investigators considered twin and triplet births together. The number of triplet and quadruplet births seems too small to have a significant influence on the average. The observed differences are probably due to geographical variations.

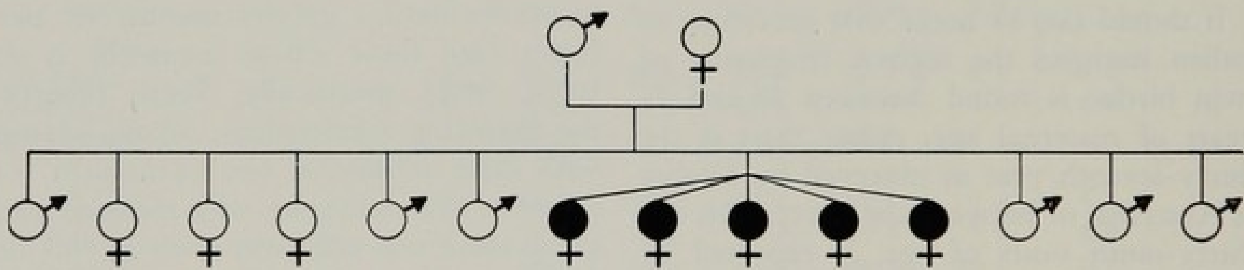
Most certainly, however, the age of the mother plays an important part in determining twin births, beyond the effect it normally has on all births. This conclusion would seem to be justified since the average maternal ages at which twins and single births are produced do not correspond at all. In any case, increasing age is a contributing factor to the occurrence of DZ twin pregnancies, although Dahlberg's estimate, that twin pregnancies among women 35 to 40 years old are three to four times as likely as among those who are 20 to 25 years old, seems too high.

It is difficult to ascertain the manner in which the age factor operates. As a mere hypothesis, there is Prinzing's theory of age causing disturbances in the implantation and segmentation of the fertilized egg. In the course of a more detailed study on menstruation, Škerlj (1939) investigated the possible relationship between menarche and the birth of twins. Using Norwegian subjects, he classified menarche in the following way: *early* when it occurred before 13.5 years of age; *medium* (normal) between 13.6 and 15.5; *delayed* when it occurred at or after 15.6 years of age.

Applying this classification to his material Škerlj found that women with early menarche have a greater number of twin births than those whose menarche is delayed. More specifically, Škerlj observed the following relationships: among women with early menarche, one twin birth was found in 65.6 deliveries; with medium menarche there was one twin birth in 70.3 deliveries; and with delayed menarche there was one twin birth in 93.3 deliveries.

Another maternal characteristic, possibly related to age but different in nature in that it is essentially functional, has also been used to explain the genesis of twinning; namely, the proliferative capacities of the mother. That this theory should attract the attention of gemellologists is understandable. It is quite common to find twin pairs in large families; that is, born to mothers with a high fertility.

This impression is strengthened by the observation of families in which various combinations of twins with single-born



Figs. 41 and 42. The Dionne Family.

Table XXIII

FREQUENCY OF TWIN BIRTHS ACCORDING TO MATERNAL AGE AND NUMBER OF PREGNANCIES (Duncan)

Classification of Pregnancy	*Pregnancies per Maternal Age Group*			*Twin Pregnancies per Maternal Age Group*			*a/b Quotient*		
	25-29	30-34	35-39	25-29	30-34	35-39	25-29	30-34	35-39
2nd to 4th	3,235	1,628	568	20	19	9	162	86	63
5th to 7th	766	1,568	993	6	27	17	128	58	58
8th to 10th	28	283	616	1	7	19	28	40	32

children offer striking examples of familial fecundity. In one case described by Berger and recorded by Engelhorn a woman produced 36 children in 30 pregnancies. Another illustration is the Dionne family, where the quintuplets were preceded by six single births, and followed by three other single births, making a total of 14 children (Figs. 41 and 42). Equally remarkable was the fecundity of a woman who had ten single and seven twin deliveries. In this family, which was studied by the author and Rédeky (Fig. 43), it turned out that there had also been notable fecundity in the ancestors.

The theory of fecundity as a factor in twinning was approached in a number of ways. The chief method was to find out whether and to what extent the frequency of twin births was influenced by the number of preceding births, and whether the actual fecundity preceding twin pregnancies was in any way connected with this occurrence. The flaw in this procedure is that the woman's fecundity is related only to the period preceding the twin birth and not to her complete reproductive period.

Nevertheless, this method was used by many authors, under the influence of Duncan's statistical data which are reproduced in Table XXIII. These figures show that the frequency of twin births is higher when the number of preceding births is greater. For example, one twin pregnancy is found in every 63 children when it is the second, third or fourth pregnancy of mothers between 35 and 39 years of age. However, there is one twin delivery in every 32 children when the birth is the result of the eighth or tenth pregnancy of mothers of the same age. The frequency is doubled in proportion to the increasing number of preceding births.

On the other hand, Australian statistics, which had previously been helpful in classifying the influence of maternal age on the

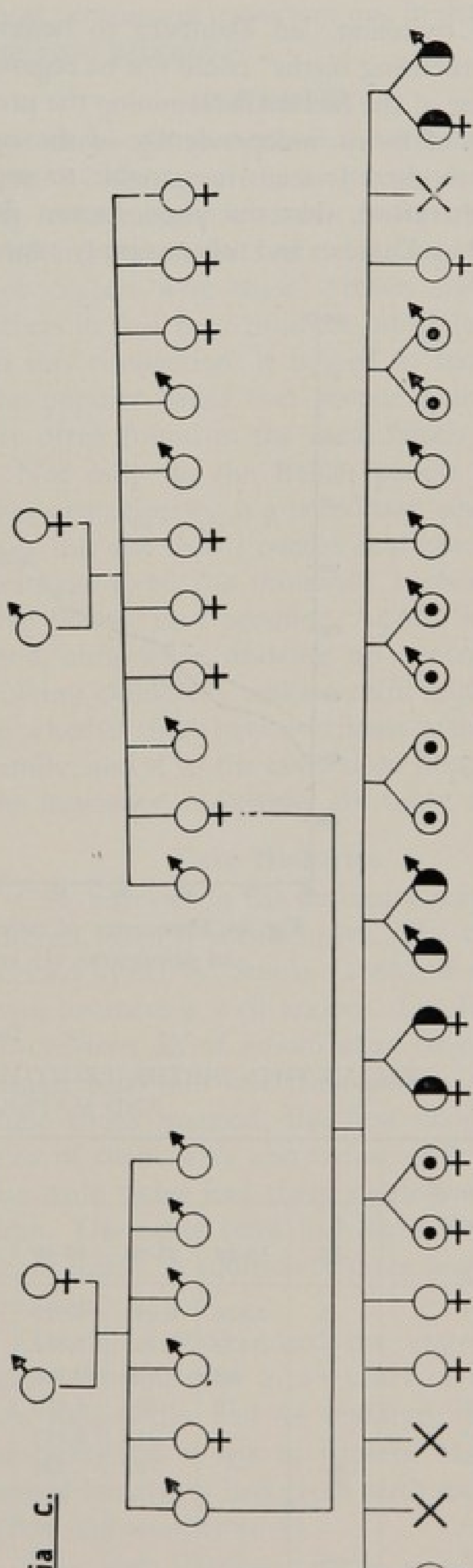


Fig. 43. Philoprogenitiveness in Family C (Gedda and Rédeky).

rate of twinning, led Dahlberg to believe that "preceding births" could not be regarded as one of the factors determining the production of twins, independently of the age of the mother. It seems reasonable to suppose, therefore, that the phenomenon described by Duncan and others simply represents an epiphenomenon of the maternal age, and not an index of some additional factor of gemellogenesis, since it is very natural that primiparae on the average are younger than multiparae.

As Dahlberg observed, women who are pregnant for the second time are on the av-

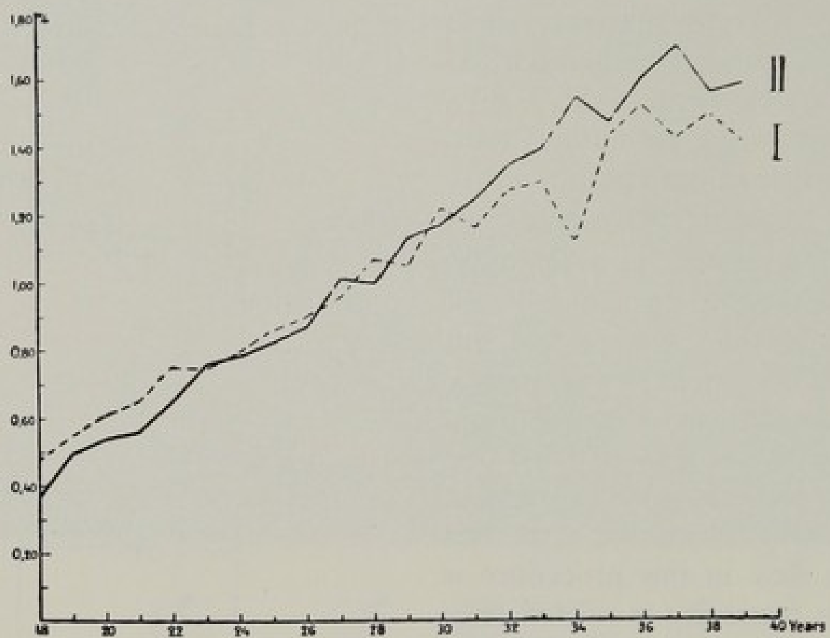


Fig. 44. Frequency of twin births in per cent related to the age of primiparae (I) and multiparae (II) (Dahlberg).

Table XXIV

ITALIAN TWIN BIRTHS (LEGITIMATE), ACCORDING TO ORDER OF BIRTH AND MATERNAL AGE (1930-1937)

Order of Birth	*Maternal Age*										*Total*
	-15	15-20	21-24	25-29	30-34	35-39	40-44	45-49	50-	*not indicated*	
1°	3	2,052	6,921	6,679	2,631	1,081	208	15	2	7	19,599
2°	—	479	3,755	6,845	3,734	1,485	259	11	1	4	16,573
3°	—	88	1,809	6,195	5,278	2,632	499	13	3	2	16,519
4°	—	16	596	4,073	5,653	3,481	726	29	—	3	14,577
5°	—	—	148	2,151	5,109	4,126	942	39	2	6	12,523
6°	—	—	30	791	3,500	3,765	1,050	43	2	6	9,187
7°	—	—	8	257	1,938	3,297	1,115	38	7	3	6,663
8°	—	—	—	78	923	2,121	1,013	41	1	1	4,178
9°	—	—	—	36	511	2,790	2,433	181	6	2	5,959
not indicated	—	2	6	12	8	7	3	—	—	2	40
Total	3	2,637	13,273	27,117	29,285	24,785	8,248	410	24	36	105,818

erage certainly older than those who conceive for the first time; women pregnant for the third time are older than those who conceive for the second time, etc. In Dahlberg's diagram (Fig. 44), compiled from Australian statistics (1908-1923), it can be seen that the higher or lower number of preceding births does not bear any perceptible influence on the frequency of twins.

The line representing twin frequency is essentially the same for primiparous mothers of twins as it is in twins' mothers who had previously had other children. Dahlberg concluded, therefore, that the fact that the number of preceding births has no influence on the frequency of twins, also indicates that the mothers of twins are not more fecund.

Italian twin data related to the number of births preceding the twin pregnancy were analyzed by the author, who based his results on the number of legitimate multiple births over a period of eight years (1930-1937), classified according to order of birth and age of mother at the time of confinement (Table XXIV). The results confirm not only that there is a greater frequency when the mother is between 30 and 34 years of age, but also that multiple births are more frequent in primiparae. It may be stated, therefore, that the number of preceding births has no positive influence on twin frequency.

All in all, the most plausible conclusion is that while theoretically a higher potential fecundity in the mothers of twins cannot be excluded, no adequate statistical evidence is available for the theory that these women are really more prolific. If there is an increase of twin frequency with a corresponding increase in the number of preceding births, it is not an expression of greater fertility. Of the various factors, only the age of the mother may be considered the most certain and important one in determining twin pregnancy.

HEREDITY

A thorough analysis of the influence exerted by the age of the mother in determining twin pregnancies has been made by studying the mothers of twins. Yet this does not explain why these women are unlike others in that they produce multiple births. In this connection, it is well to remember the popular belief that several twin births are often found in the same family.

Not only do the Italian people believe that gemelliparity is a hereditary phenomenon, but also that it occurs in alternate generations. Even the insurance agencies take this theory into account. Agents in England, also, when drawing up contracts involving childbirth, make careful inquiries as to whether there have ever been twins in the family, and if so the conditions imposed by the insurance companies are more severe.

Case Histories

Case histories in the literature may be of interest, even if inconclusive. The case described by A. W. Stocks (1861) of married twin brothers is well known. The first had 10 children, all of whom were twins (four female pairs and one male pair); seven of these twins married; the first children of four of them were also twins, while one of the male twins had three single-born children. The other twin had eight twin sons (four pairs), in addition to three single-born children.

Geissler (1896) noted the case of Dr. Mary Austin, who in 33 years of married life supposedly had 44 children: 13 pairs of twins and 6 sets of triplets. Moreover, one of her sisters had given birth to 26 children, and another to 41.

Boer and Valenta (1902) reported the case of Helm, one of female quadruplets, who married a twin and had 11 confinements with a total of 32 children, consisting of two sets of quadruplets, six sets of triplets and three pairs of twins. The father of this woman had been a twin, while her mother, one of quadruplets, was said to have had 48 sons. According to Ahlfeld, some of the details of this case may have been exaggerated in order to assure the poor woman of the sympathy of the Viennese.

Berretta-Giuffrida (mentioned by Chiarugi) placed on record the case of a Sicilian woman who had 22 twin pregnancies with

Fig. 45. American father of three single-born children and two sets of triplets (inset).

Fig. 46. The W. Family with three pairs of twins, all born in the month of October (1945, 1946, 1947).

Fig. 47. Monozygotic twin sisters in a Tulsa hospital with their dizygotic sets of twins and the proud grandmother.

two husbands. Another example, described by Apert (1919), is that of a fellow named Brunet who fathered 21 sons in seven pregnancies in his marriage plus an additional pair with a maidservant.

Also remarkable were the cases of double triplet pregnancies reported by Hornstein (1918), Uthmöller (1922), and Breipohl (1937). In Hornstein's case, the two births were so close together that in a period of one year the mother had six sons.

Greulich (1938) described the case of a woman who gave birth to six pairs of twins, all diagnosed as DZ by the fetal-membrane and similarity methods. Her pregnancies resulted in twins and nontwins in the following order: ♂, ♀♂, ♀♀, ♂♀, ♀, ♀♂, ♂, ♂♂, ♂♀. It may also be noted that her father had a set of triplets with his second wife.

In 1948 a stir was created by an Irish woman living in Syracuse, New York, who gave birth to her first set of triplets when she was 35 years old, and had a second set five years later. Altogether, she had nine children, all of whom enjoyed good health (Fig. 45).

Equally unusual is the case of an American fisherman whose wife gave birth to her first pair of twins in October of 1945, eight months after her wedding day. The couple had another pair of twins in October of 1946, and still a third pair in October of 1947—making a total of six children in three years (Fig. 46).

In 1947 twin sisters, described as monozygotic (Fig. 47), each gave birth to twins in the same hospital, only a few days apart. Both sets were of opposite sex. No less remarkable were the B. family shown in Figure 48 (one set of quadruplets, one set of triplets, and four pairs of twins), and an American family studied by Keeler and Getting (28 instances of multiple births in a total of 300 individuals).

In view of the foregoing reports, it is reasonable to assume that there is some genetic mechanism operating in the etiology of twinning, although no experimental data are available in man to substantiate this theory.

ETHNIC - GEOGRAPHIC VARIATIONS

The observation of higher twin frequencies in the Northern than in the Southern districts of France was ascribed by Puech to ethnic fertility differences between the two regions (1874). In 1902 Weinberg also suggested that differences in the frequency of DZ twins found between German-Austrian populations on the one hand and various Latin and Slavic populations on the other might be explained on the grounds of some ethnic variation.

Diverse theories have been advanced for such regional fluctuations in frequencies. The simplest one implied different and

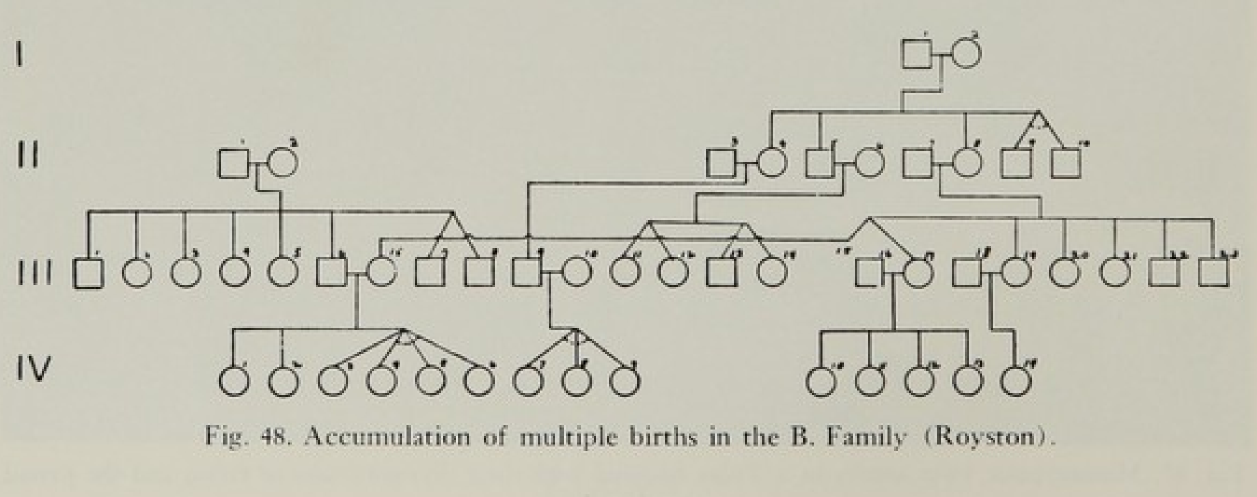


Fig. 48. Accumulation of multiple births in the B. Family (Royston).

sometimes inadequate techniques in registration, although this argument would not seem to hold water for more recent statistics. Another theory was based on differences in the average marriage age for women, as dictated by local custom. The tendency towards earlier marriages in Southern Europe, and later ones in Northern Europe, might conceivably have an effect on the frequency of twin births in view of the previously discussed connection between multiple births and maternal age. While such a relationship cannot be ignored, it has been considered by some authors as insufficient to explain the total range of geographical variations in twin frequency.

For instance, Prinzing (1907) showed that the average marriage age of a woman does not vary proportionally to the variation in twin frequency. Noting increased twin frequencies in the Northern districts of France, Germany and Italy, he doubted that an ethnic factor could be precluded, especially for dizygotic twins. It seemed to him that the frequency of multiple births was low among the Latins, medium among the Slavs, and high among the Finns and the Germans.

In dealing with such geographical variations, Dahlberg (1926) also denied that they could be explained by differences in the average marriage age of the females, since similar variations were found in populations without corresponding age differ-

Table XXV

DIFFERENTIAL RATES OF MULTIPLE BIRTHS IN THE UNITED STATES, ACCORDING TO AGE AND ETHNIC STATUS OF THE MOTHER (*Vital Statistics*)

	Total No. of Births	*Single Births*	*Total No. of Multiple Births*	*Twins*	*Triplets*
White Mothers—All Ages	100,000.0	98,984.8	1,015.2	1,005.7	9.2
10-14 Years	100,000.0	99,668.9	331.1	331.1	0
15-19 Years	100,000.0	99,450.4	549.6	546.5	3.1
20-24 Years	100,000.0	99,225.2	774.8	769.8	4.8
25-29 Years	100,000.0	98,980.2	1,019.8	1,010.8	8.7
30-34 Years	100,000.0	98,689.3	1,310.7	1,295.7	14.4
35-39 Years	100,000.0	98,410.7	1,589.3	1,569.9	19.4
40-44 Years	100,000.0	98,707.3	1,292.7	1,281.2	11.4
45-49 Years	100,000.0	99,279.0	721.0	721.0	0
50 Years and Over	100,000.0	100,000.0	0	0	0
Colored Mothers—All Ages	100,000.0	98,729.8	1,270.2	1,250.8	19.0
10-14 Years	100,000.0	99,913.7	86.3	86.3	0
15-19 Years	100,000.0	99,361.6	638.4	635.6	2.8
20-24 Years	100,000.0	98,971.4	1,028.6	1,022.7	5.9
25-29 Years	100,000.0	98,464.8	1,535.2	1,517.1	18.9
30-34 Years	100,000.0	98,057.3	1,942.7	1,887.8	52.6
35-39 Years	100,000.0	97,865.6	2,134.4	2,079.9	54.4
40-44 Years	100,000.0	98,230.7	1,769.3	1,714.4	54.9
45-49 Years	100,000.0	98,449.6	1,550.4	1,550.4	0
50 Years and Over	100,000.0	100,000.0	0	0	0

ences. In a special study of twin frequencies as associated with maternal age, he found certain differences that could be attributed only to differences in the ethnic characteristics of the populations involved. However, subsequent statistics were inconclusive. Nevertheless, there are various indications that geographic variations in twin frequencies may be due to the effect of some ethnic factor. Neefe's finding of a higher frequency of multiple births among Catholics than among Protestants was probably another expression of ethnic factors.

Statistical data collected by American authors have thrown further light on the question of geographical variation. Inasmuch as the United States is a nation where different ethnic groups live together under comparable environmental conditions, it is ideal for studying this subject. Thus, for example, Benedict (1928) was able to identify the reason for differences in basal metabolism among students at the University of Boston. Apparently, the average recorded in the white population was quite different from that noted in the colored population.

Of similar significance was the finding of American investigators who noted an increase in the rate of twin births in colored populations over that in the white. This observation indicated that some specific ethnic factor was responsible for geographical variation, and that latitude, along with the climatic as well as other changes associated with it, plays only a secondary role at best.

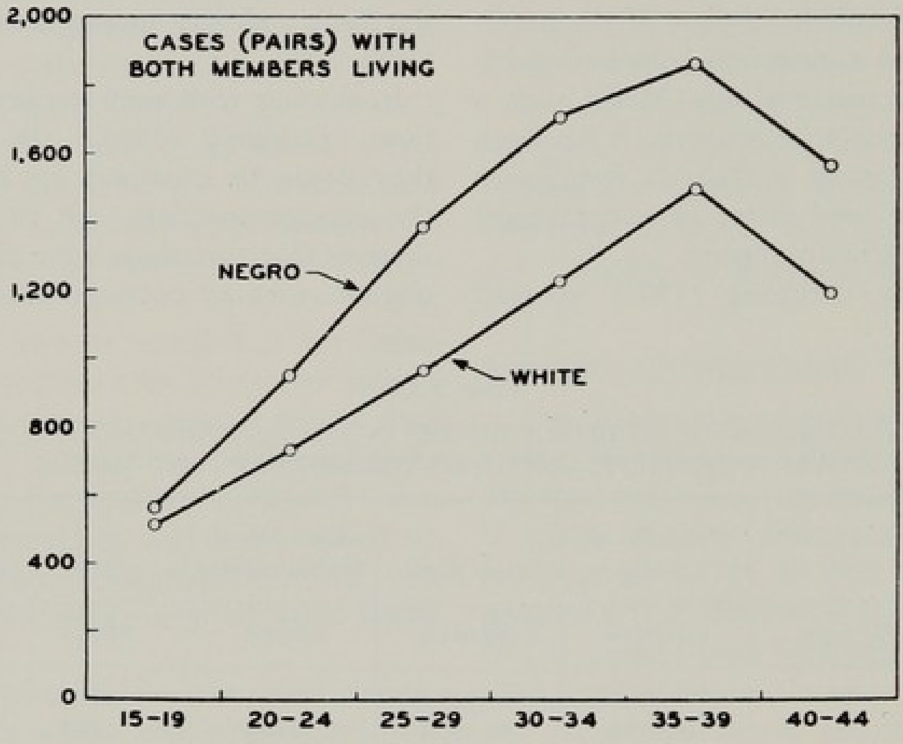


Fig. 49. Ethnic differences in the frequency of surviving twin pairs in the United States in 1944 (Vital Statistics).

An analysis of twin births in the U.S.A., considering both ethnic factors and maternal age, was presented in *Vital Statistics* (1947) on the basis of random birth statistics per 100,000 (Table XXV, Fig. 49). Again, a higher frequency of twins and triplets was shown in the colored population as compared to that in the white population. Irrespective of this quantitative difference, the age of the mother most favorable to twin production in both samples proved to correspond to the age group 35-39.

MacArthur (1942) also regarded variations in the incidence of twins as ethnically determined. He assumed, however, that a relationship exists between the bodily characteristics and the frequency of DZ twins. Consistent with the finding that multiple births are most frequent in Northern Europe, where the average height of the people is greatest, he observed that in the United States, too, the two areas with the largest number of twins are (a) Kentucky, where the population is tall, and (b) the Northern border states, where many Scandinavian immigrants live. Similarly, the Negroes, especially the American Negroes whose forebears were chosen by slave traders chiefly for their good physical qualities, seem to be distinguished by a high frequency of twin births.

Since many ethnic characteristics are determined and perpetuated in the species by the laws of heredity, to label a biological trait as "racial" means that it must somehow be gene-controlled. Obviously, therefore, any evidence classifying the twinning phenomenon as a racial characteristic more or less confirms its hereditary causation. This causal relationship, already indicated by the concentration of twin births in some families, is corroborated by the observation of ethnic variations.

FAMILY DATA

Accepting the genetic theory of the twinning phenomenon as the most plausible explanation, we may proceed from discussion of ethnic group differences to more systematic family data. In 1902 Weinberg presented the first results of his comprehensive studies of the subject. Using birth statistics for Stuttgart and four adjacent villages, he compared the families of the mothers and fathers of twins, not only with respect to the total number of twin births but with respect to the ratios of single births to twin births. In addition, he related the rates of twin births in twin families to the number of births occurring in the total population.

Using more extensive data in his second study (1909), Weinberg hypothesized the existence of a specific recessive factor possessed by the mothers of DZ twins and their families. On the father's side he found a twin rate of 1.87% among the mothers whose sons had had twins. This finding of a genetic twinning factor transmitted by the father was a contradiction of the author's earlier statistics and was later questioned by Dahlberg (1926). In particular, Weinberg's theory on MZ twins was considered too complex.

Table XXVI

FEMALE RELATIVES OF THE MOTHERS OF TWINS (Weinberg)

Relationship to Mothers of Twins	*Same-Sex Twins*			*Opposite-Sex Twins*		
	Number of Persons	*Number of Births*	*Number of Multiple Births*	*Number of Persons*	*Number of Births*	*Number of Multiple Births*
Mothers	579	3,970	61	254	1,848	45
Sisters	575	2,579	55	201	1,022	24
Daughters	833	3,430	44	323	1,464	27
Total	1,987	9,979	160	778	4,334	96

While supporting Weinberg's theory with respect to a genetic factor in the mothers of DZ twins, Dahlberg was skeptical as to the genetic basis of MZ twinning. Different views were held by Melmann (1910) and Bumm (1912), as well as by Mayer (1914).

The importance of the father in transmitting the twinning attribute was also stressed by Gall and Brattström (1914). The latter investigator reported the history of a Russian peasant, Wasilieff, who married twice. His first wife presumably gave birth to four sets of quadruplets, all of whom lived, seven sets of triplets, and 16 pairs of twins. His second wife had two sets of triplets and six pairs of twins—a grand total of 87 children, 84 of whom lived. In his report, Brattström mentioned another family, that of a workman who had 82 children with two wives.

In 1916 Danforth studied the frequency of twin births in 50 Midwestern families. Among the brothers of the mothers of twins he found a 1:32 ratio between twins and single births, while among the brothers of the twins' fathers the ratio was 1:37. Danforth concluded, therefore, that the factor for DZ twinning is inherited only through the female line, but that an MZ twinning factor may be transmitted by both parents.

In 1919 Bonnevie studied a Norwegian family that yielded a rate of 7.7% twin births. Using Weinberg's differential method, she found that 80% of these twins were dizygotic. She therefore agreed with Weinberg in assuming a genetic factor only for two-egg twins, apparently transmitted by the mother. Even when there were twins on the paternal side or the father was himself a twin, Bonnevie succeeded in demonstrating that there were twin births in the mother's family, too.

While the Weinberg-Bonnevie theory postulated the existence of a recessive gene

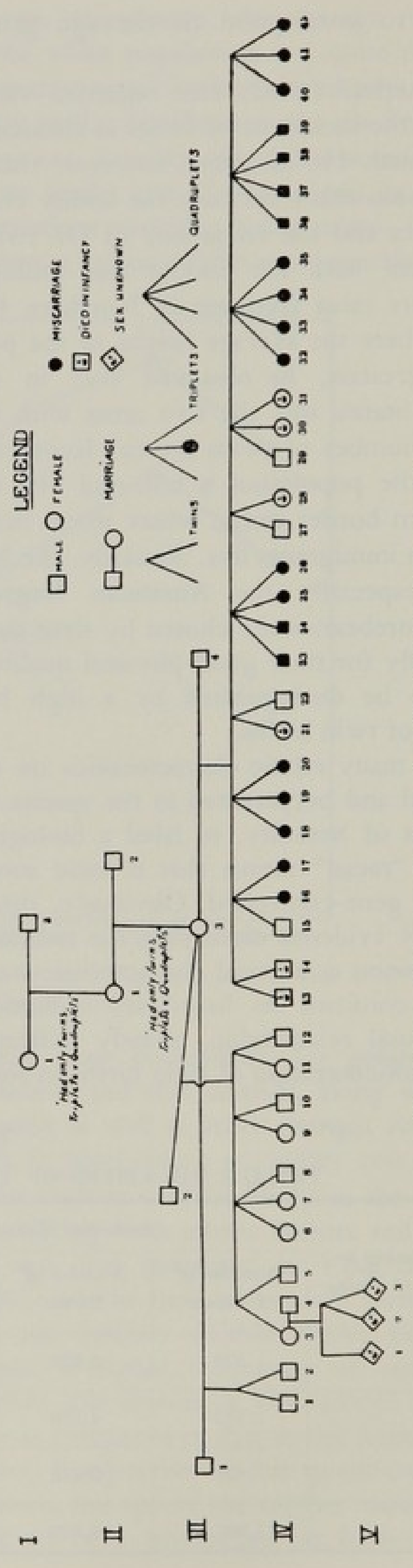


Fig. 50. Familial concentration of multiple births (Davenport).

for twinning only with respect to the mothers of dizygotic twins, Davenport believed in a hereditary factor for both types of twins, transmitted not only by the mother but by the father as well. As far back as 1919 Davenport observed a tendency to an unusual concentration of multiple births in one family (Fig. 50). There had been twins in four successive generations, and one woman did not have a single-born child with any of her three husbands. Instead, she had 15 sets of twins, triplets and quadruplets.

In 1920, Davenport studied 30 mothers who had given birth to more than one pair of MZ twins. He found that the sibs of these mothers (the brothers and sisters) had 10 sets of twins in a total of 77 births. In the families of the fathers, 5 pairs of twins were found in a total of 38 births. Thus a figure of 13% for the frequency of twins was obtained for both the sibs of the mothers and those of the fathers.

Davenport also studied the families of couples who had two or more pairs of either MZ or DZ twins. In the group of the mothers, he found 16 pairs of twins (4.5%) in 355 births. Among the offspring of the fathers' mothers, there were 12 pairs of twins (4.2%) in 289 pregnancies. By means of additional data on the sibs of the fathers and mothers of twins, Davenport obtained in the families of twins a rate of twin births which was 4 to 7.5 times greater than that of the total population (estimated at 1.1%).

Davenport's data included 15 pairs of MZ twins from a total of 195 births distributed with equal frequency in the families of both fathers and mothers. Hence he assumed the operation of a genetic factor for both types of twins. He also concluded that there was no significant difference in the effect exercised by the father or the mother, at least in families with two or more pairs of twins. It may be mentioned, however, that while, in Dahlberg's opinion, Weinberg was at fault in having omitted some twin births from his calculations, Davenport may have made the opposite mistake of omitting some single births.

In another analysis (1927), Davenport collected data on the grandchildren of persons derived from a total of 865 multiple births in 200 families. In the families of the female twins there were 22.7% twin births, and in those of the males, 21.7%. Moreover, the frequency with which the wives of the male twins produced twins was higher than that of married women in general.

Davenport thus confirmed the importance of paternal heredity in the production of twins. He believed that while double ovulation is common, it results in a twin birth only in every fifth case, because of the presence of a lethal element contained in the sperm. The hereditary mechanism of twinning on the father's side would be instrumental in eliminating the effect of this lethal component.

In another family described by Peiper (1923), the importance of the genetic factor in the male was evidenced by the fact that the man, who was a twin, had nine pairs of twins with his wife. However, when this woman married a second time, she gave birth to six sons, all of whom were single-born.

Bonnevie's theory of a single-recessive factor for twinning in the mothers of twins was confirmed by Wehefritz (1925). However, because of the manner in which the latter collected his DZ twins, his statistical conclusions were criticized. In any case, his study showed that in some families the ratio of mothers of twins to mothers of single-born children is 1:3.8 (24:109 mothers, or 40:153 if Bonnevie's families are added). Therefore, the operation of some Mendelian factor was assumed by Wehefritz. Other authors were of the same opinion, including

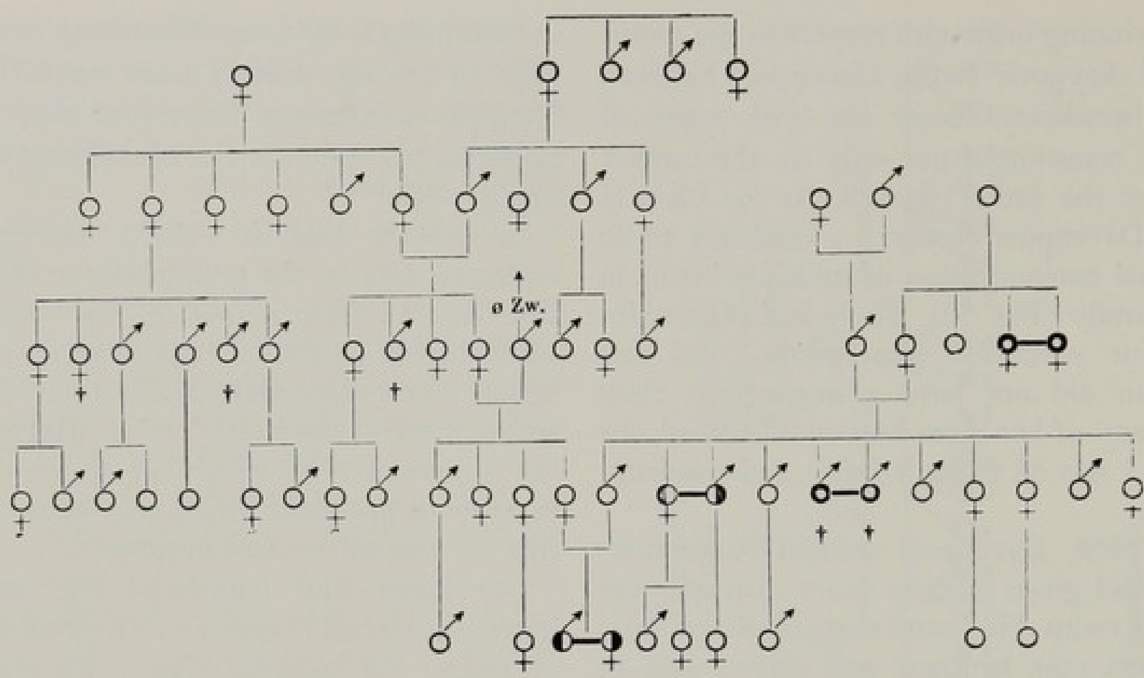


Fig. 51. Accumulation of multiple births on the paternal side of the family (Curtius).

Hofsten (1919), Lenz (1923), and Siemens (1923), the latter two with respect to DZ twins only.

In 1927 Curtius reinvestigated the subject in a series of 30 families. His main interest was the question of whether the father was as important as the mother in the production of twins. To prove his point, he described seven pedigrees in which the fathers of twins came from families clearly carrying the twinning trait, while no evidence of this kind was found in the ancestry of the mothers.

The most remarkable of Curtius' pedigrees is shown in Figure 51. The multiple births recorded in these pedigrees included one set of MZ triplets, one set of MZ twins, and five pairs of DZ twins. Curtius' belief in a genetic basis for one-egg twinning was at variance with Weinberg's hypothesis, but was confirmed by v. Verschuer genealogically (9 pedigrees).

The genetic theory was supported (a) by a statistically significant increase in the number of twins among the close relatives of one-egg twin index cases; (b) by the occurrence of both types of twins in the same families (8 pedigrees), as well as in the same sibship (2 case histories); and (c) by the observed combination of both zygosity types within a set of quadruplets in one family, and of MZ twins within a set of dissimilar triplets in another. Curtius assumed, therefore, that the tendency to twinning is determined genetically and by the same genetic factor for either type of zygosity.

This view was shared by Dahlberg (1930), who concluded from his own data (birth records of a stable Scandinavian population, 1860-1900) that mothers bearing a tendency to produce DZ twins also have the tendency to produce MZ twins. In this study, the mothers of twins (with a total of 2,222 births) were found to have had a twinning rate of $5.56 \pm 0.49\%$. Thus, where a woman had a tendency to have twins, her chances of really having them was estimated at 6%, or one set of twins in 17 births.

As to the relationship between MZ and DZ twinning, Dahlberg obtained data on the mothers of opposite-sex twins. While the rate of DZ births was about four times as high as in the general population (4.48 ± 0.9%, as against an expected 1%), the frequency of MZ twins was found to be 2.24 ± 0.99%. Although this increase was not statistically significant, the investigator considered it highly suggestive. He also hypothesized that at least one out of every 10 women carries the genetic factor for twinning.

Similar conclusions were drawn by v. Verschuer (1932), who collaborated with Curtius in a study of 931 twin families. The results of this study were as follows:

1. No difference was found between the brothers and sisters of the parents of twins in regard to the tendency to produce twins. A moderate increase was observed only in the sisters of the mothers of opposite-sex twins.

2. The brothers of the fathers of twins tended to produce twins with the same frequency as the brothers of the mothers of twins.

3. The tendency to produce twins was observed in the brothers of the parents of MZ and DZ twins to almost the same degree. It was found to be slightly lower in the families of MZ twins.

4. One-egg and two-egg twins occurred with the same frequency in the families of MZ and DZ twins (either same-sex or opposite-sex).

Somewhat different views were expressed by Greulich (1934), who studied 495 parental couples with at least one pair of twins (93 MZ pairs, 121 same-sex DZ, 152 opposite-sex DZ, 129 undiagnosed). The rate of twins born to these mothers was 2.99 ± 0.039%, as compared to a frequency of 1.84% for the total U.S. population.

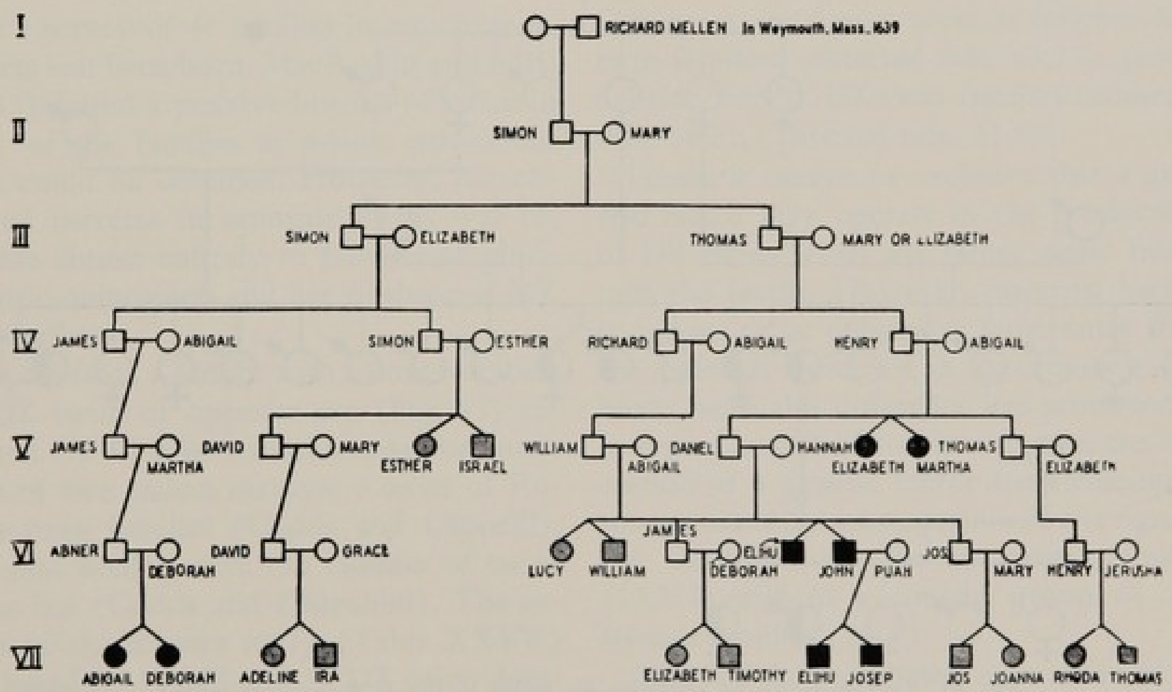


Fig. 52. Transmission of twinning by males in the M. Family (Mellen).

From these findings Greulich concluded that the parents of twins are more likely (92.1%) than would be expected by chance to produce twins, but he thought that parents of DZ twins differed from those of MZ twins in their twin-producing ability. In his opinion, the former had twins much more frequently than foreseeable had twinning been due to chance, while the latter presented a frequency of twin births just barely above chance expectations. Hence he came to the conclusion that MZ and DZ twinning phenomena were either entirely independent of each other or differed in several etiologic respects.

Of interest in this connection is also Mellen's report (1938) on the M. family, in which no twins were produced in three generations (Fig. 52). In the following four generations, however, ten pairs were born, all on the male side of the family. The next three generations were again unproductive of twins, very much to the dismay of the

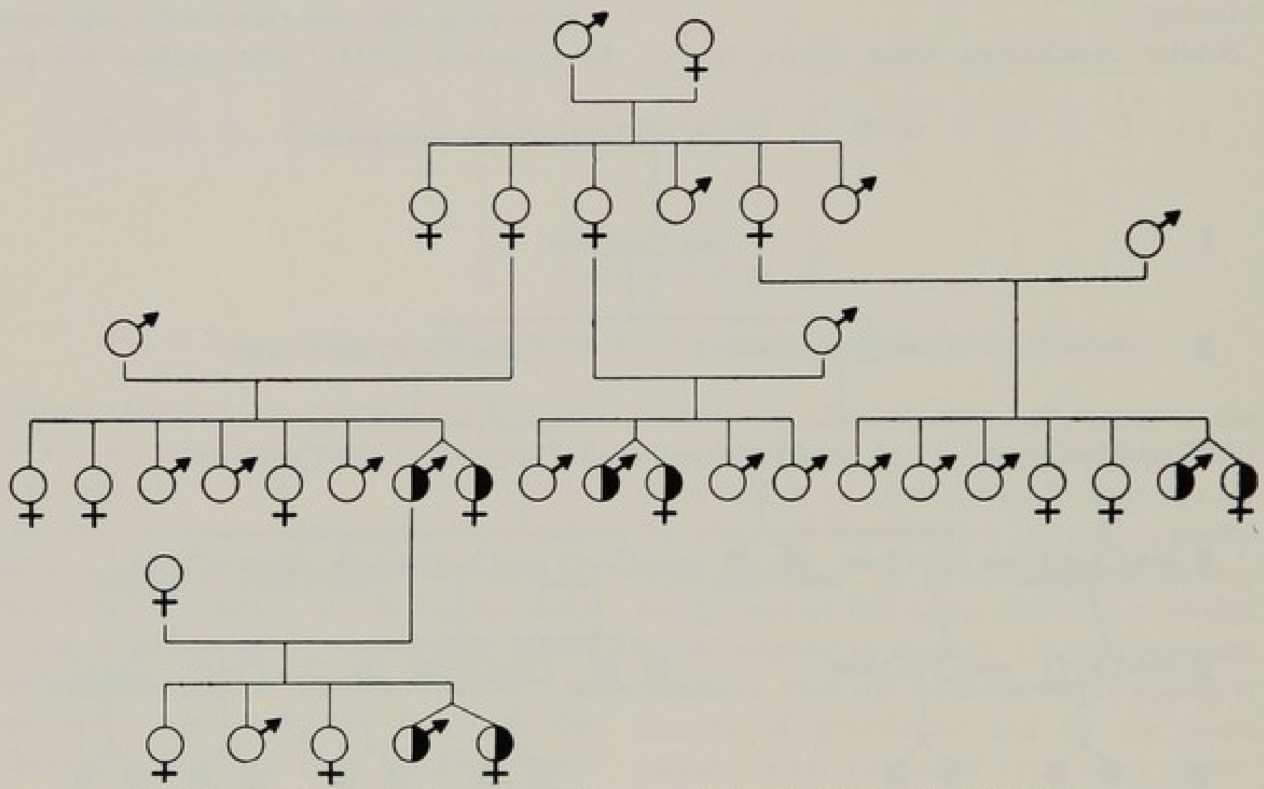


Fig. 53. Accumulation of opposite-sex twins in the B. Family (Gedda).

Table XXVII
DISTRIBUTION OF TWINNING IN 110 ROMAN TWIN FAMILIES

Twin Families Investigated	*Proportion of Families*				*Families with Additional Twins*							
	With Additional Twins		*No Known Instances of Other Twins*		*Maternal Side Only*		*Paternal Side Only*		*Both Sides*		*Relationship Unknown*	
	Number	*Per Cent*	*Number*	*Per Cent*	*Number*	*Per Cent*	*Number*	*Per Cent*	*Number*	*Per Cent*	*Number*	*Per Cent*
MZ (51)	41	80.4	10	19.6	18	43.9	13	31.7	8	19.5	2	4.9
DZ (59)	44	74.6	15	25.4	25	56.8	9	20.5	5	11.4	5	11.4
Total (110)	85	77.3	25	22.7	43	50.6	22	25.9	13	15.3	7	8.2

author who was unable to offer a plausible explanation for the procreative inconsistencies in this family.

The genetic problems of MZ and DZ twinning were also studied by Southwick (1939) in a series of 919 families, and by Slater (1939, 1948) in 462 families with both MZ and DZ twins. Both investigators concluded that the two zygosity types were based on the same genetic factor. In addition, Slater postulated that this factor may be carried by the female as well as the male.

In a survey of 45 families in which quintuplets had been born, MacArthur and Ford (1937) found a positive history of twins in 54% of the families in which anamnestic data could be obtained. However, the observed increase in multiple births was referable almost entirely to families of plurizygotic quintuplets and not to those of MZ quintuplets.

Apart from a family with a concentration of DZ twins of opposite sex (Fig. 53) reported by Gedda, mention may be made here of two Italian surveys: a series of Roman twin families (Gedda and Cappelli), and one dealing with the families of twins from Iesi (Gedda and Cherubini). The results of the Roman study (Table XXVII) are based on 51 MZ and 59 DZ pairs. Altogether, additional twins were found among the relatives of 85 cases (77.27%). The given rate was slightly higher in the families of MZ twins (80.43%) than in those of DZ twins (74.57%). Unconfirmed twin reports were disregarded.

The difference in percentage between the sexes was as follows: On the maternal side, additional twins were found in about half the cases (50.58%), and on the paternal side in only one quarter of the cases (25.88%). If families with twins on both sides were included, the given percentages increased to 65.9 on the maternal side, and to 41.2 on the paternal side.

Another difference became apparent when the families of MZ and DZ twins were compared. While the operation of the twinning factor revealed itself on the mother's side for both types of twins, there were quantitative differences. In the families of MZ twins, additional twins were found in 43.9% of the families on the maternal side, and in 31.7% on the paternal side. In the families of DZ twins, the given percentages were 56.8 and 20.5, respectively, if families with twins on both sides were excluded. Otherwise, the figures were as follows: MZ twin families: maternal side, 63.1%; paternal side, 50.9%. DZ twin families: maternal side, 68.2%; paternal side, 31.8%.

Hence it cannot be excluded that a genetic factor may operate in the production of DZ twins when the father alone transmits the factor. However, maternal heredity seems to be of greater importance than the paternal influence in determining DZ births, with this difference less pronounced in regard to MZ births. In any case, the operation of a genetic factor for twinning is substantiated by a comparison of the figures for additional twins in twin families (77.3%) and in a control group of 100 Roman families (23%).

The Iesi data are based on a series of 66 pairs of twins and their families. In this study, relatives were found to have given birth to twins in 45 cases (68.2%). A comparison of the maternal and paternal groups of relatives yielded the following results: Other cases of twins only on the maternal side, 43.9%; other cases of twins only on the paternal side, 13.6%; other cases of twins on both sides, 10.6%.

Despite some differences between the statistics for the families of twins in Rome and in Iesi, the main point at issue was confirmed by both studies. It may be stated, therefore, that the twinning phenomenon shows a clearly familial pattern, which means that it has a genetic basis. Apparently, both sexes are able to transmit this genetic factor which operates in MZ as well as in DZ twinning. Of particular significance in this respect are families and sibships with both zygosity types. An interesting pedigree of this kind is shown in Figure 54.

In conclusion, it would seem that the phenomena of MZ and DZ twinning are based on the same genetic factor. However, various exogenous or endogenous concomitants may be responsible for one or the other type of twin pregnancy in a given family. Similar circumstances may determine the degree of multiparity in a certain sibship.

Among the concomitant influences, maternal age is certain to play a role. Apparently, the age factor tends to increase the production of DZ twins and other multiples, although it is clear that this factor has an effect only on the phenotypic expression of a character that is determined *genotypically*.

An attempt has been made in this chapter to demonstrate that *twinning of both types has a genetic basis*. The following sections will be devoted to a discussion of how this hereditary trait operates in the parents of twins; how it becomes manifest in the phenotype; and how it determines the various types of multiple birth.

Chapter VI

THE GENETICS OF TWINNING

As HAS BEEN SHOWN, the basic cause of twinning is genetic in nature. At the current stage of development of genetics, both general and applied to twins, it is possible to go into the question of how the transmission of the trait takes place. From the time scientists first became interested in the problems presented by human twins, the possibility that twinning had an hereditary origin has been considered. In the pre-Mendelian era, Goelert (1870) theorized along the following lines. On the basis of data on 132 twin pairs, he suggested that twinning might be hereditary (transmitted either directly or indirectly), and that it tended to be increased by inbreeding.

Modern genetics began with this century, or, more precisely, with the rediscovery of mendelian laws. Research in this field was inspired by a belief in the heredity of twinning. Weinberg was the first to show that gemelliparity was genetically determined, although he supported two theories that are now obsolete. One held that the hereditary factor was not present in MZ twins, but only in DZ twins. The other implied that, in the genealogy of DZ twins, the male side has only the function of transmitting the hereditary factor, and plays no part in the mechanism which determines twinning as such. The production of twins was assumed to depend exclusively on the ability of the female to produce more than one ovum for simultaneous conception.

In 1908 Weinberg suggested that the given hereditary factor was of the recessive type. Other investigators who took an interest in the genetics of gemelliparity at that time included Oliver (1912), Friedenthal (1914) and Meyer (1917).

Bonnevie's study of a Norwegian peasant family (1919) led to the discovery of a 3.5% rate of twins, instead of the expected 1.3 to 1.4%. She concluded from this observation that the tendency to twinning may be increased in some sibships. As to the parents of twins, it could also be shown that either the father or the mother or both had twins among their relatives and might have transmitted the trait. Since there were many consanguineous marriages in the given family (39.7% of all marriages observed), it was assumed, by analogy rather than statistical analysis, that twinning is based on a recessive genetic factor.

In 1920 Davenport advanced the hypothesis that polyovulation (assuring the simultaneous presence of two ova), the prerequisite for the production of DZ twins, is a common occurrence. That twin pregnancies are not likewise common was explained by the operation of *lethal factors* in the spermatozoa. In matings lacking such lethal factors, the tendency to twin pregnancies is greater. By pointing out this lack of lethal factors in the spermatozoa of some males, Davenport was acknowledging the father's role in the production of DZ pregnancies.

Under the influence of Weinberg's theories, Wehefritz (1925) believed that a genetic factor operates only in DZ twins, endowing predisposed women with the ability to produce more than one ovum at a time.

Variations in the manifestation of the trait were explained by different combinations of random factors at the time of conception. According to Wehefritz, homozygosity for twinning can be effective only in the female; the male may be a homozygote for the same factor, but cannot express it because he does not possess the appropriate organ. This would then be a *sex-limited* factor which, in line with the theory of Bonnevie and others, is classifiable as recessive.

Among those who challenged Wehefritz' theory was Dahlberg (1926), who insisted on the genetic origin of both MZ and DZ twins. In his opinion, regardless of whether these tendencies were independent of each other or somehow connected, the ability to produce twins was assumed to be of the same nature in the two sexes—in ovum as well as sperm. In females this tendency would sometimes produce a dizygotic and sometimes a monozygotic pregnancy. The sperm would give rise only to MZ twins. Only in a monozygotic pregnancy could inheritance be demonstrated on the father's side.

Curtius (1927) also believed in the paternal transmission and recessiveness of the twinning factor, but he rejected the theory of sex-limitation. He remarked that Wehefritz had overlooked the fact that in 12 of his 14 families apparently the father transmitted the tendency to produce twins. In particular, there was one family where the father of twins came from a family with several sets of twins, while his wife came from a family in which there had been no twins in four generations.

In 1933, with the collaboration of v. Verschuer, Curtius, working with a series of 931 pairs of twins, reinvestigated the question of a recessive factor expressed in a homozygous state in both sexes. They came to the following conclusions:

1. Two essential conditions which favor homozygosity of a recessive trait are often encountered in the families of twins: familial endogamy (marriage between consanguineous subjects) and inheritance from both parents. Of 50 pairs studied, no additional twins were found in ten families, while there were twins on the father's side in eight, on the mother's in 16, and the remaining 16 pairs showed twins on both sides.

2. Twins are frequently produced by members of large sibships at a rate approximating the 25% expected in a recessive trait. Curtius' material included a sibship of 12 brothers (two unmarried), one of eight brothers (two unmarried) and one of nine brothers (one unmarried). In each of these sibships, two brothers demonstrated their ability to produce twins.

3. Additional twins are frequently found in the collateral lines rather than in the direct ancestors, as is typical of recessive traits. In Curtius' series there were eight families showing this principle.

In 1938 Cantoni studied several generations of a small but highly consanguineous population of an alpine village in Italy. Among other factors, he observed an unusual frequency of twin births. There were 24 twin pairs in 1,038 births, i.e. 2.36 twin births in every 100 deliveries or 42 single births for every twin delivery. In addition, the investigator found that twins are usually conceived in cold weather and are apparently the result of a single recessive factor.

Subsequent studies of the genetic aspects of twinning included those by Komai (1936), Southwick (1939), MacArthur (1942) and Slater (1948). In Slater's opinion, both sexes may transmit the two types of twins. Twinning is not less frequent among the cousins of twins than it is among parents and children. It is more frequent in cousins than among the uncles, aunts, nephews and nieces. This distribution is not easily explained solely on genetic grounds. Slater assumed that the genetic factor has a high penetrance and is widely distributed in the population, but he questioned the genetic nature of the main etiological factors.

The general impression conveyed by the literature may be set forth as follows: While it seems clear that the basis for the phenomenon of twinning is genetically determined, chiefly because there is an accumulation of twins in certain families, the same cannot be said for the other aspects of twinning. Although many observers favor a recessive mechanism, others point to irregular dominance with low penetrance. A third theory suggests that penetrance may be high, but that the factor for twinning depends on a number of nongenetic conditions which may precipitate or hinder its expression.

Of course, this hypothesis does not preclude the essentially genetic basis of twinning, since even those nongenetic influences assumed by Slater act only or principally in certain families. One may say, therefore, that the theory of a genetic factor for twining, although thrown out the door, returns by way of the window. To be sure, all this uncertainty as to the genetic mechanism of twinning leaves the field wide open for future research, but an attempt will be made here at least to delineate the problem.

It is unclear whether the factor for twinning, termed *doubling tendency* by English authors and *Spaltungstendenz* by the Germans, follows a single-factor or multifactor type of inheritance. Nevertheless, the factor is known to be transmitted by the female as well as the male, although with different frequencies, both for MZ and DZ twins and sometimes by the same genotype for all these variations.

Labelling this tendency the "G factor" (G for Gemellus or Geminus = twin), we are inclined to believe that its manifestation is primarily related to the organism of the parent (ovogenesis and spermatogenesis). Were the expression of the G factor connected with the filial generation, that is, the zygote, we could explain the development only of MZ but not DZ twins. Regarding the first alternative (parental organism), if the twinning factor is inherited either from the father or the mother we should postulate a dominant and not a recessive mechanism, as some observers seem to indicate. In other words, by affecting the organism of the parent (probably through gametogenesis), the G factor would produce a potential mother or father of twins.

The female organism would then have the ability either to form ova of different genic composition at the same time (DZ twinning with maternal inheritance), or to form ova capable of initiating a division of the zygote upon fertilization (MZ twinning with maternal inheritance).

In the male organism, the G factor would somehow induce certain spermatozoa to effect a double pregnancy (dizygotic twinning with paternal inheritance), or would enable them upon fertilization to produce the gemellogenetic division of the zygote (MZ twinning with paternal inheritance).

Provided these hypotheses can be substantiated, it is understandable that the different ways of transmission (paternal or maternal), or the production of the two types of twins resulting therefrom (MZ or DZ), may be variously combined. On this basis it would be possible to explain why certain families with only MZ or DZ twins display both familial similarity and dissimilarity in the genetic process. We recall a family with several multiple births, all of which were of opposite sex and therefore dizygotic. The transmission of the trait seemed to have taken place in three instances through the female side and through the male in one (Fig. 53, p. 88). We also take note of another family in which both MZ and DZ twins were born (Fig. 54).

number of genes, two genetically identical individuals could occur only very rarely by chance. Certainly, this event would be far less frequent than the number of identical twins found in the general population. Friedenthal estimated that genetic identical-

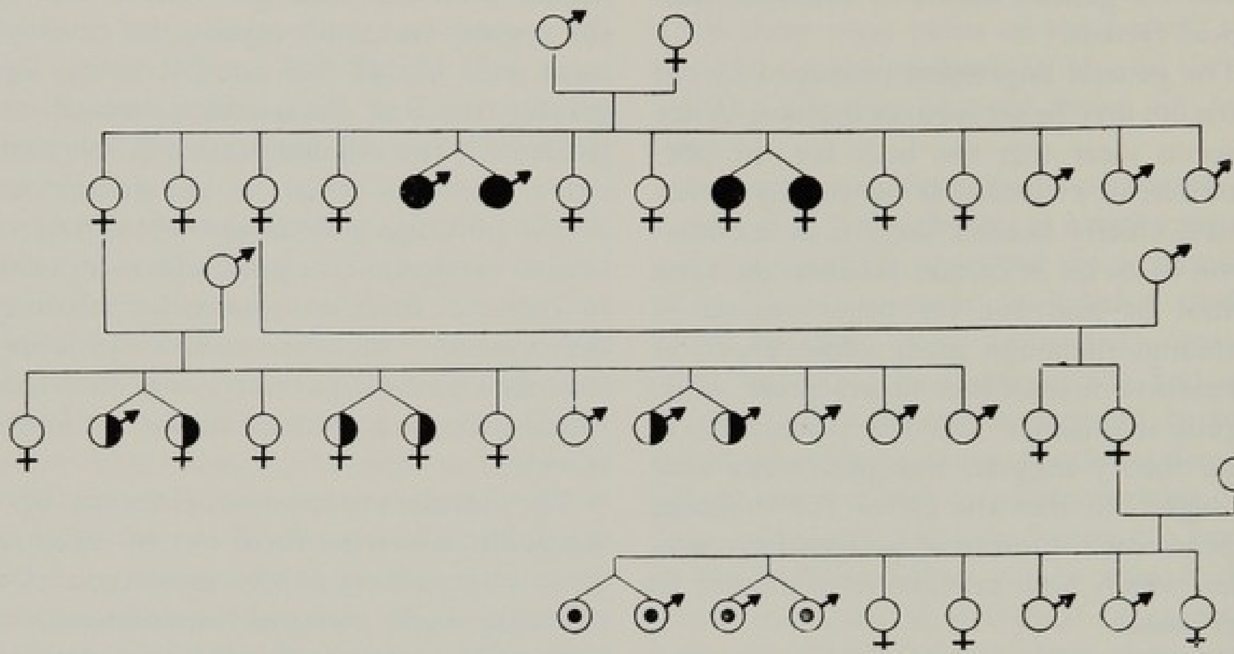


Fig. 54. Accumulation of MZ and DZ twins in an Italian family (Gedda and Rédeky).

ness of two brothers derived from two zygotes could be expected only once in the astronomical figure of 200,000 trillion fecundations. Hence Curtius' comment that "such a perfect resemblance, based on complete concordance with respect to several polygenic systems, is conceivable only in individuals who are genotypically alike."

The importance of such nongenetic influences as maternal age, low rate of metabolism, nutrition, climate and the like cannot be disregarded but it would seem that they are effective only in favoring or suppressing the action of the G factor.

Whether the production of MZ and DZ twins represents the effect of one or two genetic traits, there can be no doubt that the two types of twins clearly differ from each other on a genetic basis.

While geneticists disagree in identifying the genetic factor involved, the consensus, based on anatomical evidence, is that similar twins derive from a single zygote and dissimilar twins from two separate zygotes.

Proof of the derivation of identical twins from a single zygote is supplied by the laws of probability. In view of the vast

In Zazzo's opinion, segregation of the 48 chromosomes of each parent actually allows a multitude of combinations equal to the 24th power of two, i.e. exactly 16,777,216 combinations, raised by the mating of the parents to several hundred billions. We are dealing here, as Zazzo put it, with variations on the same theme; the 48 chromosomes derived from a single pair of parents. The theme, however, varies from one couple to another. . . . One may add that this estimate considers neither the vast number of genes located on the chromosomes, nor their exchange during the process of meiosis.

On this mathematical basis, all geneticists today are agreed that a multiple birth can give rise to two or more MZ individuals (triplets, quadruplets and so forth) who possess one genotype. While it is inaccurate to speak of phenotypical identity (outside influences always cause some differences, however slight, between MZ twins), the identity referred to is genotypical. From a phenotypical point of view, MZ twins are to be classified as "similar" and DZ twins as "dissimilar."

While the genetic identicalness of MZ twins is generally accepted, as is the genetically determined difference between MZ and DZ twins, similar certainty cannot be attached to the idea that DZ twins are derived from two different ova. For instance, Danforth (1916), Curtius (1927) and others suggested that the secondary oocyte may form two cells capable of being fertilized by two different spermatozoa. Such twins would have an identical maternal inheritance but a different paternal one, and would be "intermediate between normal MZ and DZ pairs as to their degrees of similarity" (Greulich).

This hypothesis is based on histological evidence in animals, but the lack of reliable data in man forces us to conclude that a distinction of two types of DZ twins is at best premature. In our opinion, but on different grounds, it would be desirable to divide DZ twins into two subgroups, thus making it possible to speak of a "third type" of twins. The details of this classification will be discussed in a subsequent chapter. Here it may be stressed, with no reflection intended on any other hypotheses, that the study of genetics has to rely on established facts, i.e. on the primary division of twins into monozygotic and dizygotic pairs. This scheme does not preclude further subdivisions, and is preferable to the descriptive term "identical twins" or the obstetrical term "monochorionic twins" which may be misleading.

The genotypical equality of MZ twins is the starting point for the twin study method, which presupposes that their intrapair differences are due to nongenetic influences. This principle, although generally valid, has its limitations. For one thing, the expression of genes varies, especially that of so-called "weak genes," which produce minor effects, and the penetrance may be too low to insure their phenotypical appearance in both twins. For another, there is the possible occurrence of mutations in one twin sometime during his life.

Regardless of the environmental conditions MZ twins may encounter either together or separately, their gene-specific traits usually tend to remain unchanged and continue to be identical in both individuals. Hence the extraordinary similarity of MZ twins, often so perplexing to outsiders. Even the children's mother is often at a loss to tell her MZ twins apart and has to resort to natural or artificial identification marks, called *distinctions* (see chapter on methodology in Vol. II).

Guttmacher reported that domestic animals, such as dogs, despite their keen sense of smell, are also deceived by the similarity of MZ twins. The similarity of hereditary characters in MZ twins remains pronounced even where there is mixed parentage, as was described by Wagenseil (1930) for twin sisters who were partly European and partly Micronesian and had been reared in entirely different environments.

If more than two individuals are the result of a multiple birth, there may be any combination of the two types of twins. Genetic studies of triplets have shown that they may be monozygotic, as was true of

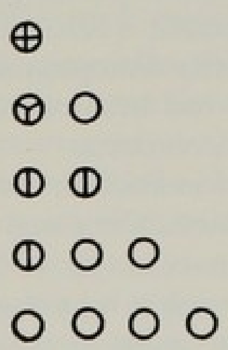
Fig. 55. Japanese MZ triplets aged 9 (by Komai and Fukuoka).

the cases described by Hartmann (1923), Gates (1929), Clarke and Revell (1930), Komai and Fukuoka (1931, Fig. 55), v. Verschuer (1932), Anderson, Forrest and Scheidemann (1932), Sanders (1932), Sontag and Nelson (1933), Buschke (1935), and Gardner and Rife (1941). Triplets derived from two zygotes have been reported by Rowe (1928), Anderson, Forrest and Scheidemann (1932), Buschke (1935), and Gardner and Rife (1941). Case histories of trizygotic triplets have been placed on record by Anderson, Forrest and Scheidemann (1932), Buschke (1935), and Gardner and Rife (1941, three sets).

The four types of zygosity in quadruplets are described in the following list provided by Newman and Gardner (1942):

In the opinion of Newman and Gardner, the occurrence of Subgroup B of Type II is improbable, although Lotze (1937) and Sarkar (1943) classified the Derner quadruplets as the result of two MZ pairs. A number of cases of quadruplets reported in the literature and studied with respect to zygosity are listed in Table XXVIII.

It may be mentioned here that the zygotic similarity or dissimilarity alluded to in distinguishing the two types of twins refers chiefly to Mendelian characteristics transmitted by genes (chromosomal material) and not to other modes of transmission. Cytoplasmic inheritance, for instance, is more obscure and may behave in a different way, and in certain DZ twins may produce



Type I: monozygotic quadruplets.

Type II: dizygotic quadruplets:

Subgroup A: Three MZ quadruplets plus one single birth.

Subgroup B: Two pairs of MZ quadruplets.

Type III: trizygotic quadruplets:

Two MZ quadruplets plus two single births.

Type IV: quadrizygotic quadruplets:

Four single births.

Table XXVIII

ZYGOSITY OF SAMPLE QUADRUPLET SETS

Name	Country	Date of Birth	Sex	Zygosity	Bibliography
Gale	U.S.A.	?	♀♀♀♀	⊕	J. Hered., 1935
Morlok	U.S.A.	1930	♀♀♀♀	⊕	Clarke, 1932, MacArthur J.W., Mac Arthur O.T., 1937 Gardner and Newman, 1943
Kaspar	U.S.A.	1936	♂♂♂♀	☮ ○	Gardner and Newman, 1943
Derner	Germany	1927	♀♀♀♀	⦶ ⦶	J. Hered. 1935, Lotze 1937, Sarkar 1943
Keys	U.S.A.	1915	♀♀♀♀	⦶ ○ ○	J. Hered., May 1916, J. Hered., Oct. 1916, Gardner and Newman, 1940
Badgett........	U.S.A.	1939	♀♀♀♀	⦶ ○ ○	Sinclair 1940, Gardner and Newman, 1942, Pryor 1948
Gehri...........	Switzerland	1880	♂♂♀♀	○ ○ ○ ○	Schlaginhaufen 1940
Perricone.....	U.S.A.	1929	♂♂♂♂	○ ○ ○ ○	Gardner and Newman, 1940
Schense........	U.S.A.	1931	♂♂♀♀	○ ○ ○ ○	J. Hered., 1939, Gardner and Newman, 1944

a marked degree of genetic similarity not derived from nuclear material.

The pronounced differences in gene-specific characteristics observable in dissimilar twins are a definite indication of different genotypes. In other words, two separate fertilizations gave rise to two zygotes which differ in their assortment of genes. It is justifiable, therefore, to call these twins dizygotic, irrespective of whether they are derived from one or two ova.

Concerning the dissimilarities of DZ twins, it may be pointed out that while there is complete genotypical concordance in MZ twins, the degrees of discordance in DZ twins are only relative. Their genic constitutions are also distinguished by the fact that DZ twins have the same father and the same mother. According to the laws of probability, at least half the genes an individual receives from his parents through alternative sets of gametes must be alike in two brothers with the same father and mother. This statement refers to characteristics which show individual variability, i.e. those outside of the common traits distinguishing the species, the ethnic group, or the family.

The general genetic specifications of MZ and DZ twins are so distinct that they provide the best method of distinguishing one variety from the other. Any study of twins has to begin with diagnosing the zygosity of a given pair. This diagnosis is no longer based on an examination of the fetal membranes, but on a comparison of the relative degrees of similarity or dissimilarity in hereditary characteristics. The diagnosis obtained from the twins themselves is vastly superior to a diagnosis established obstetrically. Examination of the fetal membranes, which will be discussed later, gives merely a general idea, but provides no real evidence. MZ twins are not always monochorionic and DZ twins are sometimes not dichorial. These facts are taken into account by the *polysymptomatic similarity method* developed by Siemens and v. Verschuer (see chapter on methodology in Vol. II).

As experience has shown, the characteristics compared in this procedure are quite resistant to outside influences and are transmitted according to schemes that have been firmly established by genetics. In essence, it is the genetic analysis of two phenotypes that makes it possible to determine whether a given pair of twins is derived from one or two zygotes.

THE TWIN STUDY METHOD AS USED IN HUMAN GENETICS

Particularly appropriate here is Wood's statement (1919) to the effect that twins prove the importance of chromosomes. No better proof exists of the genotype's vital function than the fact that MZ twins remain similar throughout their lives, even in widely different environments. Methodologically, therefore, twins render valuable service to the science of genetics.

In studying the transmission of characters in plants and animals and also in man, geneticists depend on the experimental method (cross-breeding, induced mutations, and the like). Ever since Mendel's experiments with plants, the most important results in this young branch of science have been obtained in this fashion. For obvious reasons, of course, the experimental method cannot be used when it comes to the human species. Therefore, three main approaches remain open to workers in human genetics: the purely statistical method, the family history method, and the twin study method.

The research potentialities afforded by the family history method are valuable but limited. Many inherited traits are rare, and most pedigrees are not extensive enough for genetic analysis. Other shortcomings are a limited number of births, uncontrolled matings, unmarried individuals, the length of human life, and the like.

These limitations enhance the usefulness of the twin study method for human genetics. The main purpose of this method is to analyze the effect of genic activity. The tendency of MZ twins to be concordant as to normal or pathological traits justifies the assumption of the gene-specific nature of the character in question; that is, of its dependence on the action of one or more genes. An assumption, of course, can only be a working hypothesis rather than proof, since numerous outside influences may also result in concordances. The causes of concordances must therefore be carefully investigated by means of one or more of the following procedures:

1. A statistically representative number of cases is required, as well as the usual tests for statistical significance.

2. Other influences which may simulate hereditary phenomena are to be ruled out, foremost among them being congenital but nonhereditary causes such as syphilis.

3. Data on MZ twins living in a given environment are to be compared with data on DZ twins for the same environment to determine the difference, if any, in concordance between the two groups. Whenever MZ pairs are concordant or show a significantly lower rate of discordance, there is reason to assume that their tendency to concordance is ascribable, wholly or in part, to the effect of gene action (genes being always the same in MZ twins, and partly different in DZ pairs).

4. Data on MZ twins reared together and living in the same environment are to be compared with data on other MZ pairs who lived apart. Phenotypical dissimilarities between separated MZ twin partners are suggestive of environmental influences, while observed similarities in the face of separation strongly support the genetic hypothesis.

Macklin and Snyder (1947) were correct in pointing out that the extent to which MZ and DZ twins differ in concordance for a given trait depends chiefly on the genotypes of the parents and on the etiologic complexity of the character in question. For example, with both parents belonging to blood group O, it is expected that all their children, whether born singly or as MZ or DZ twins, will also belong to group O. In this instance, DZ and MZ twins will show the same degree of concordance, without weakening the genetic specificity of the blood groups.

However, if one parent is heterozygous for the simple dominant condition of polydactylism, DZ twins will be only one-half as frequently concordant as will MZ twins. Again, for a trait produced by two pairs of recessive genes, and with the parents heterozygous for both, the concordance rate of MZ twins will be sixteen times greater than that of DZ twins. Therefore, observation of DZ twins concordant for a given trait does not of itself prove that the trait is not hereditary.

Another important area for the application of the twin study method is the analysis of the genetic mechanism involved. Although pedigrees are the most effective method for investigations of this kind, the study of DZ twins may also be useful, as Rife (1938) has shown in regard to single pairs of genes with or without dominance as well as for sex-linked and sex-limited factors.

In addition, the twin study method is helpful in the analysis of multifactor types of inheritance. If no discordant pairs occur among MZ twins, and if the discordance rate of DZ twins exceeds 27 percent for an autosomal trait with only two known phenotypes, it is safe to assume that more than one pair of genes is involved in producing the character in question.

Furthermore, the study of twins is productive in investigations of quantitative and qualitative variations in the phenotypical manifestation of a gene-specific trait. It is known from the studies of Timoféeff-Ressovsky and others that variability in the expression of dominant and recessive genes alters the mode of manifestation. This variability occurs in two ways: (a) in the *penetrance* of the gene, a concept which refers to the frequency with which a genetic factor is likely to express itself; and (b) in the *expressivity* of the gene, a concept referring to the degree of manifestation, i.e. the quantitative expression of the factor.

In applying the twin study method to variations in penetrance and expressivity, it is necessary to have a genetically determined trait and a series of MZ twins with both members of a pair having lived in the same environment. Of course, the greater the number of twins studied, the more reliable the result will be.

Analyzing certain hereditary conditions in this way, one will often observe discordances, when a pathological trait manifests itself in only one MZ twin. A higher concordance rate indicates a higher degree of penetrance, and a higher discordance rate points to weak genes.

This procedure becomes complicated when the visible (primary) phenotype depends on an invisible (secondary) phenotype. A situation of this kind was once assumed by Luxenburger to exist with respect to schizophrenia. However, this hypothesis has not been confirmed by other investigators.

As a rule, MZ twins show a relative rather than a perfect degree of concordance for pathological traits. For example, one twin may have all the symptoms of the condition and the cotwin only an abortive form. Such observations are common in twin pathology and when made in a representative series of cases prove very useful for analyzing quantitative variations in the expressivity of the gene.

Chapter VII

EMBRYOLOGY OF TWINNING

Despite many advances in the field of human embryology, there is still much uncertainty about the manner in which a single organism is conceived and developed. It is not surprising, therefore, that even less is known about the embryogenesis of twins, especially since the mechanisms operating in a multiple birth are not uniform. Whatever information is available on the subject does not come from direct observation but is based largely on embryological data provided by malformations of human embryos, by multiparous mammals, and by animal experiments.

It is well known that the reproductive process which in certain periods leads to the formation of male and female gametes is distinguished by a particular type of cell division called *meiosis*. This process differs from the usual type of somatic cell division or *mitosis*, which reproduces in each of the daughter cells the exact number of chromosomes contained in the mother cell. In meiosis, the chromosomes of the newly formed cells are reduced to half the original number.

As one of the fundamental problems of biology, the phenomenon of meiosis has given rise to considerable speculation. Theories advanced range from those of older investigators, such as Farmer and Moore, Schreiner, Janssens, Grégoire and others, to more recent ones, such as that of White based on studies of spermatogenesis in the grasshopper.

In accordance with Darlington's hypothesis, meiosis represents the succession of two divisions of a nucleus, accompanied by only one division of the chromosomes. Consequently, the distribution of the chromosomes in the somatic cell is in the so-called diploid form ($2n$), while the chromosomes in the reproductive cells are in the haploid form (n). Hence meiosis may be regarded as the characteristic maturational process of the gametes. Only with the halving of the chromosomes in meiosis does the number of chromosomes remain constant in each individual of the species.

Another important point is that meiosis, although remaining the same in its basic mechanism, has different significance for the maturation of male and female gametes. While spermatogenesis has no special meaning in gemellogenesis, in the reproductive process of the female the formation of the so-called polar bodies may assume a certain importance. As a rule, these bodies are eliminated, since they do not represent a female gamete and cannot be fertilized. In connection with the process of two-egg twinning, however, the possibility of a polar body being fertilized has been considered, as will be discussed later.

The union between spermatozoon and ovum, called *syngamy*, leads to the union of the male and female pronuclei, a phenomenon known as *amphymixis*. This process results in the formation of the first representative cell of the new organism, referred to as *zygote*. In some conceptions leading to the production of one-egg twins, this general mechanism is complicated by a phenomenon called *polyembryony* wherein two or more embryos are derived from a single fertilized ovum or zygote.

In dealing with the embryological problems of monozygotic and dizygotic twins in man, it would be well to bear in mind two facts regarding experimental polyembryony: (a) the artificial production of twins in certain animal species; and (b) the occurrence of double fetal malformations in the human species. Both observations will be helpful in understanding the embryological developments in human twins.

EXPERIMENTAL POLYEMBRYONY

Since its beginning at the close of the last century, experimental embryology has been occupied with the study of problems closely connected with the embryogenesis of MZ twins. Gemellologically speaking, the importance of these experiments lies in the confirmation of the fact that two or more organisms may derive from a single ovum. In other words, these investigations have provided experimental evidence for the existence of polyembryony, the theoretical prerequisite for monozygotic twinning.

To begin with, mention should be made of a series of experiments which induced virgin ova to break into fragments. This work showed that impregnation of single fragments was possible and in certain cases actually led to the formation of embryos. Carried out mainly in a type of echinoderm called *paracentrotus lividus*, these experiments consisted of shaking the eggs in water in small receptacles, or cutting them in meridian or equatorial directions under the microscope. Some of the fragments contain the female pronucleus and others do not, but all of them will develop when a spermatozoon succeeds in penetrating them (Hörstadius, 1928). Similar results were obtained in another echinoderm, the *Lytechinus*.

Fragmented ascidian eggs (*Ascidiella*) were also studied, and if the ovum was properly sectioned upon fertilization, it produced either two symmetrical embryos or two embryos with complementary defects. In similar experiments by Wilson (1903) and Zeleny (1904), the development of fragmented eggs of the *Cerebratulus* was also studied by means of equatorial, meridian and transverse cuttings. As long as the polar fragments were not too small, it was observed that all fertilized fragments gave rise to small but normal embryos.

The eggs of a ctenophore (*Beroe*), an annelid (*Chaetopterus*), a chordate (*Amphioxus*) and a vertebrate (*Triton*) were investigated in the same way, with consistent evidence that a complete ovum is not necessary for developing an embryo. In fact, even successively fertilized egg fragments tend to display segmentations, some giving rise to embryos of normal structure.

In another series of experiments, the blastomeres of fertilized eggs were treated by different techniques. They were either completely or partially separated, or made to undergo some alteration in the cleavage plane. Total separation of the first two blastomeres in the eggs of a sea urchin was achieved by Driesch (1891) by shaking the egg for a few minutes. Each blastomere developed into a normal embryo even after detachment, but the size of the embryo was reduced by half. On the basis of these results, Driesch formulated an important theory. The essence of it was that the first two blastomeres can be considered as *equally and totally potent*, and therefore capable of producing a complete organism.

It has since been found that this equivalence of the first cells of the echinoderm even extends to the stage of four blastomeres. When isolated, each of them divides into segments and develops a blastula approximating one-fourth its normal size. Upon gastrulation, the blastula gives rise to an embryo which is four times smaller than

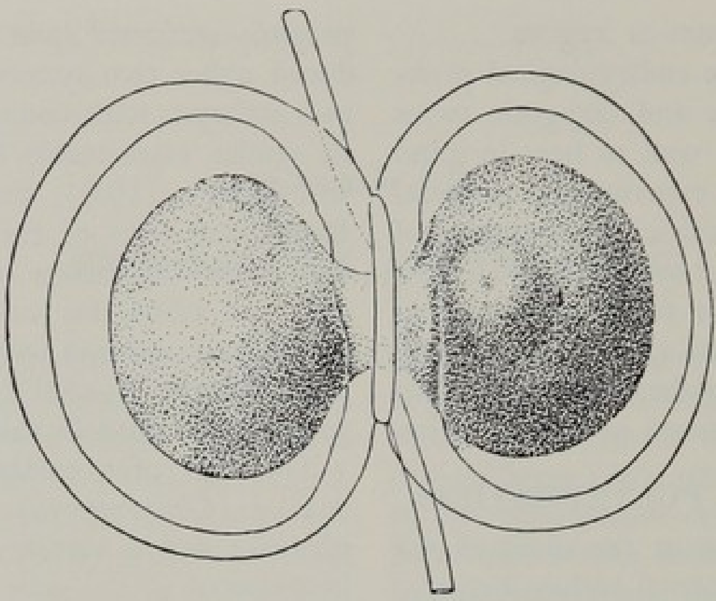


Fig. 56. Fertilized ovum of the *Triton taeniatus*, split in the middle by a hair (Spemann).

usual (Morgan). Only when eight blastomeres have been produced does the segmented echinoderm embryo lose its original total capacity. From this stage on, individual blastomeres, when isolated, give rise only to partial structures.

Herbst (1900) isolated the first blastomeres by placing fertilized sea urchin eggs in sea water from which calcium had been removed. When the isolated blastomeres were returned to normal sea water, they developed into separate organisms. Similar experiments were made by E. B. Wilson (1893) with eggs of the *Amphioxus;* by Zoja (1895) in certain medusae whose blastomeres retained their total capacity up to the stage of eight formations; by Crampton (1896) in mollusks; by Bataillon (1900) in *Petromyzon planeri;* and so forth.

In 1933 Conklin, who previously had studied the effect of centrifugation on the development of *Crepidula* eggs (1917), re-

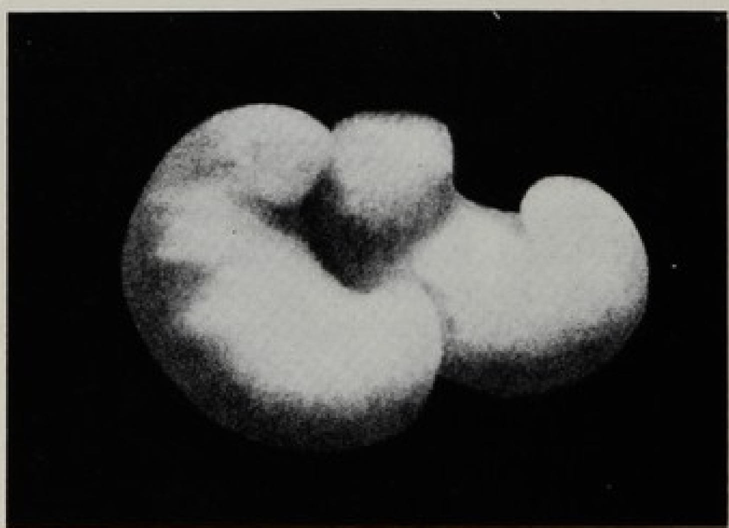


Fig. 57. Experimentally produced *Triton taeniatus* twins (Spemann).

Fig. 58. *Triton taeniatus* twins at a later stage of development (Spemann).

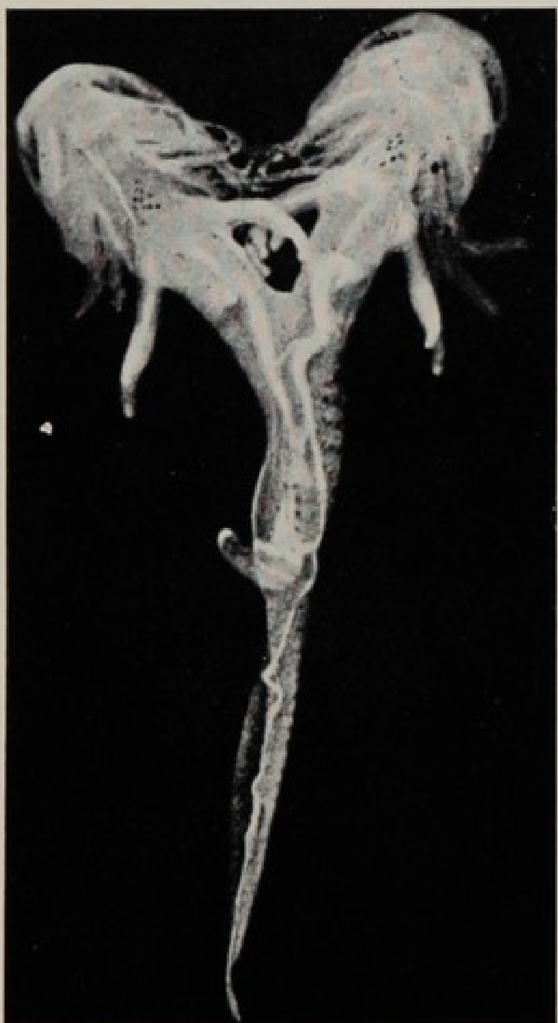


Fig. 59. Artificially produced but incompletely separated *Triton taeniatus* twins with situs inversus (Spemann).

peated Driesch's experiments on *Amphioxus* eggs damaged by shaking. He observed the development of complete organisms from isolated blastomeres, as well as the formation of two, three and four individuals variously attached to each other when the blastomeres had not been totally separated.

Another series of experiments was initiated by O. Hertwig (1893) who strangled impregnated *Triton taeniatus* eggs with a hair tied at the point of the first cleavage plane. His experiments with isolated blastomeres were continued by Enders (1895) and Herlitzka (1897), who succeeded in producing complete embryos reduced to half the normal size. In the same way, Spemann (1901-1903) experimented with triton eggs. He confirmed that twins could even be obtained from incompletely separated blastomeres. He also produced double malformations of various types: *duplicitas anterior, duplicitas cruciata* (Figs. 56-59).

An interesting phenomenon, described by Spemann, occurs when the egg, soon after impregnation, is strangled in such a way that the whole nucleus is forced into one half of the cell. At first segmentation takes place only in the nucleated half. With incomplete strangulation, however, a part of the nucleus eventually spreads into the other half, which begins segmentation at a later stage. In this manner, too, embryos may be formed which show different degrees of development (Figs. 60-63).

One of Spemann's disciples, G. A. Schmidt (1933), used the same method (strangulation with a thread) to produce twins from the fertilized egg of *Bombinator pachypus*. Other diplogenesis experiments were carried out on bird eggs. By injecting inductive organ fragments into chicken eggs which were fertilized but not yet incubated, Morita (1936-1937) obtained two embryos in 43 out of 322 cases (13.2%), and triplets or higher multiples in 12 cases (3.5%). Of the twins, 35 pairs were separated, while eight pairs were conjoined in various ways. All twins were smaller than normal embryos of the same age; most of them were shifted towards the edges of the cavities produced by the noxious action of the inductive organs. Similar changes were secured by chemical and other agents.

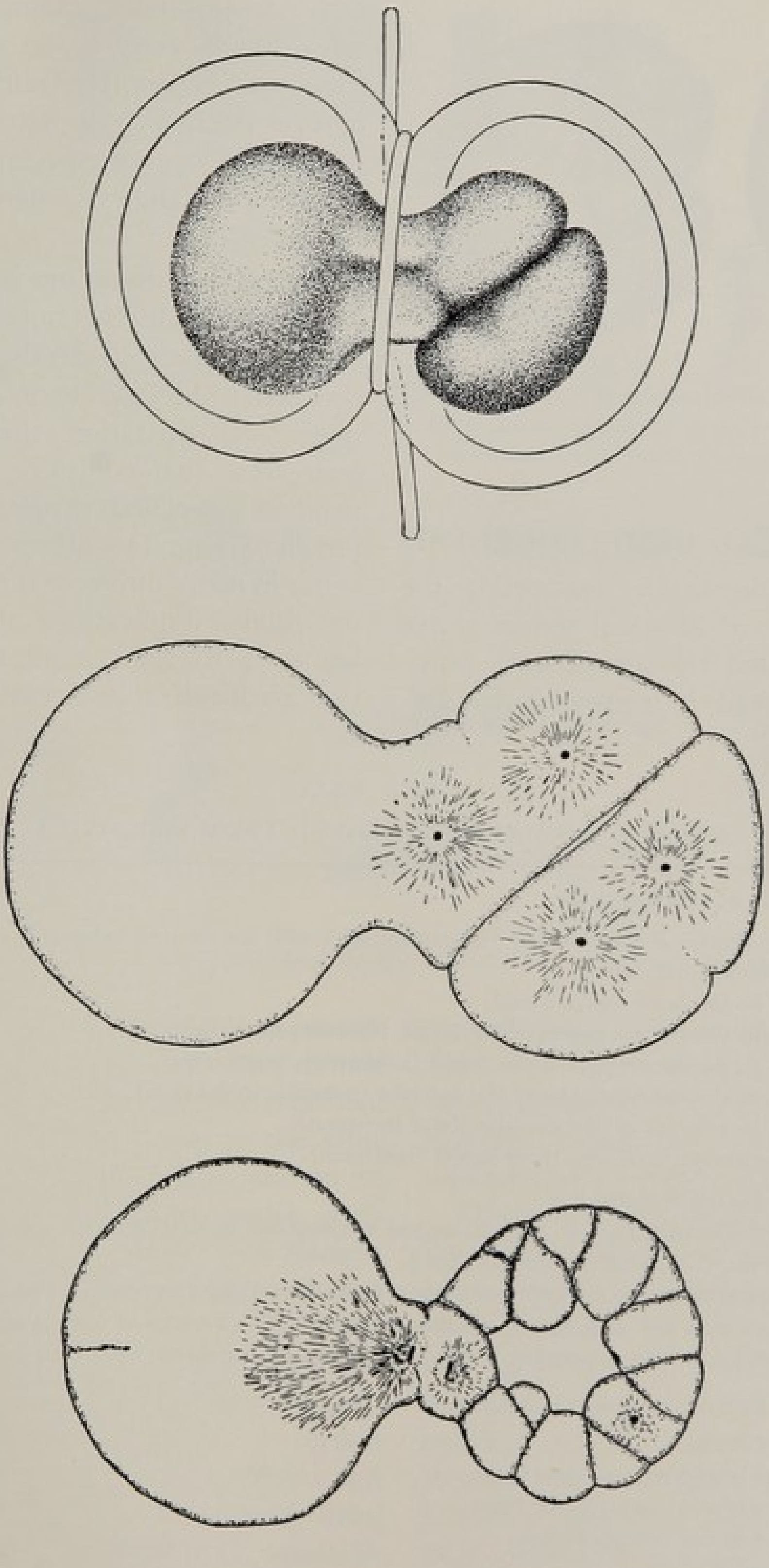
Twisselmann (1939) set lesions by electrolysis (302 cases) or micropunctured the primitive streak of chicken embryos by ultraviolet rays (94 cases). Electrolytically, he obtained the following results: 12 sets of twins and two triplets from non-incubated eggs; ten pairs of twins and one set of triplets from eggs incubated after the appearance of the primitive streak. By ultraviolet rays, three cases of asymmetric twinning were produced.

Wolff and Lutz (1947-1948) induced twinning by splitting the germ of non-incubated goose eggs with a fine glass needle. Cutting along the egg's long axis (perpendicular to the embryo's line of symmetry), they obtained a large proportion of twins facing each other head to head. If the cut was made along the egg's short axis, the twins were situated side by side, facing in the same direction. In one case, an incomplete cut led to a double malformation. Quadruple monstrosities were produced by cross-splitting, with each section of the embryonic disc resulting in a complete embryo.

From the experimental data reviewed so far, it is justifiable to conclude that fragments of virgin eggs can be fertilized and tend to be as potent as the total egg. With complete individuals derived from one or the other fragment, it would appear that the capacity of the organizer for producing ectopic diplogenetic differentiations and the responsiveness of different areas of the embryonic surface to such unusual organizational influences are of equal significance in the embryology of twinning.

Thus the experimental method confirms the observations made in animal studies of spontaneous gemellogenesis; namely, that more than one individual may develop from a single egg (polyembryony) and that the period when one-egg twinning occurs ranges from shortly after impregnation until the beginning of gastrulation. Another important finding is that the mechanism producing complete gemellogenesis may occasionally result in incomplete diplogenesis in the form of double monstrosities.

Though experimental polyembryony is effective in many different species of invertebrates and vertebrates (and in the latter from cyclostomes to birds), it would be hazardous to apply results obtained by artificial means and in an abnormal manner to a species in which twins occur as a normal developmental phenomenon. Another difference lies in the fact that in artificial gemellogenesis each separate region can give rise to a new organism, the size and weight of which however will be proportionate to the ovular fraction from which it was derived. Therefore, the new organism may be only one-half or one-quarter its ordinary size.



Figs. 60-62. Segmentation and subsequent development of the nucleated half of the *Triton taeniatus* egg after incomplete separation (Spemann).

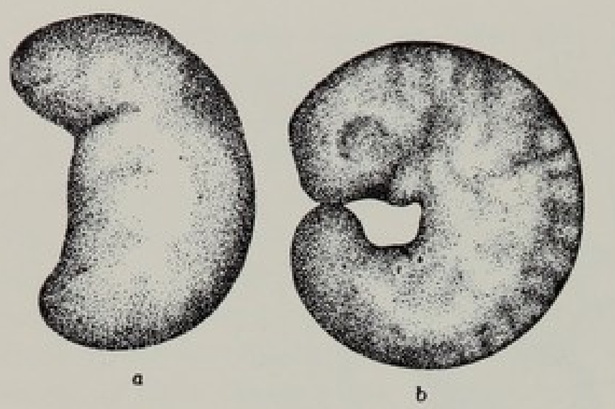


Fig. 63. Different developmental stages in artificially produced *Triton taeniatus* twins, with embryo *a* appearing younger than embryo *b* (Spemann).

TERATOLOGICAL GEMELLOGENESIS

Spontaneous phenomena supporting the uniovular theory of identical twinning are chiefly represented by spontaneous polyembryony observed in many animal species. An outstanding example of physiological polyembryony is the armadillo, as discussed in Chapter III. Another type of spontaneous phenomenon that is teratological in nature and occurs especially in the human species is the embryogenesis of double malformations.

Double malformations in man are phenotypic abnormalities resulting from the more or less complete co-development of two individuals. Showing various degrees of almost total separation, they serve to illustrate how two complete, equal and independent individuals may originate from one fertilized egg. Double malformations may occur in many different forms, ranging from the partial duplications of certain somatic segments to total duplication, producing two identical subjects connected by an or-

Table XXIX

DOUBLE FORMATIONS DERIVED FROM ONE OVUM

A. CONJOINED MONSTROSITIES
1. *Asymmetrical Double Malformations* (Heteroadelphia) with an underdeveloped *parasite* attached to a well developed *autosite*:
    a. Attached to the head (epignathus).
    b. Attached to the central region of the trunk (thoracopagus, dipygus).
    c. Attached to the dorsal part of the trunk (notomelus, pygomelus).
    d. Attached to the caudal region of the autosite (parasitic pygopagus).
    e. Attached to a cavity of the autosite (fetal inclusion).
    f. Tumor formation involving three layers (teratoma).
2. *Symmetrical Double Monstrosities:*
    a. Teratoadelphia with high or lambda-shaped conjunction (deradelphi with one head and two cervical columns, thoradelphi, ileadelphi, etc.).
    b. Teratopagi with central or X-shaped conjunction (thoracopagi, sternopagi, xiphopagi, ischiopagi, etc.).
    c. Teratodymi with low or Y-shaped conjunction (psodymi with lumbar conjunction in the psoas region, xiphodymi with conjunction in the xiphoid region, derodymi, atlodymi, iniodymi, etc.).

B. SEPARATED DOUBLE FORMATIONS
1. *Asymmetrical Twins:*
    a. Normal twin and papyraceous fetus.
    b. Normal twin and anencephalic fetus.
    c. Normal twin and acardiac fetus.
2. *Symmetrical Twins:*
    a. With phenotypic differences;
    b. Without phenotypic differences (identical twins).

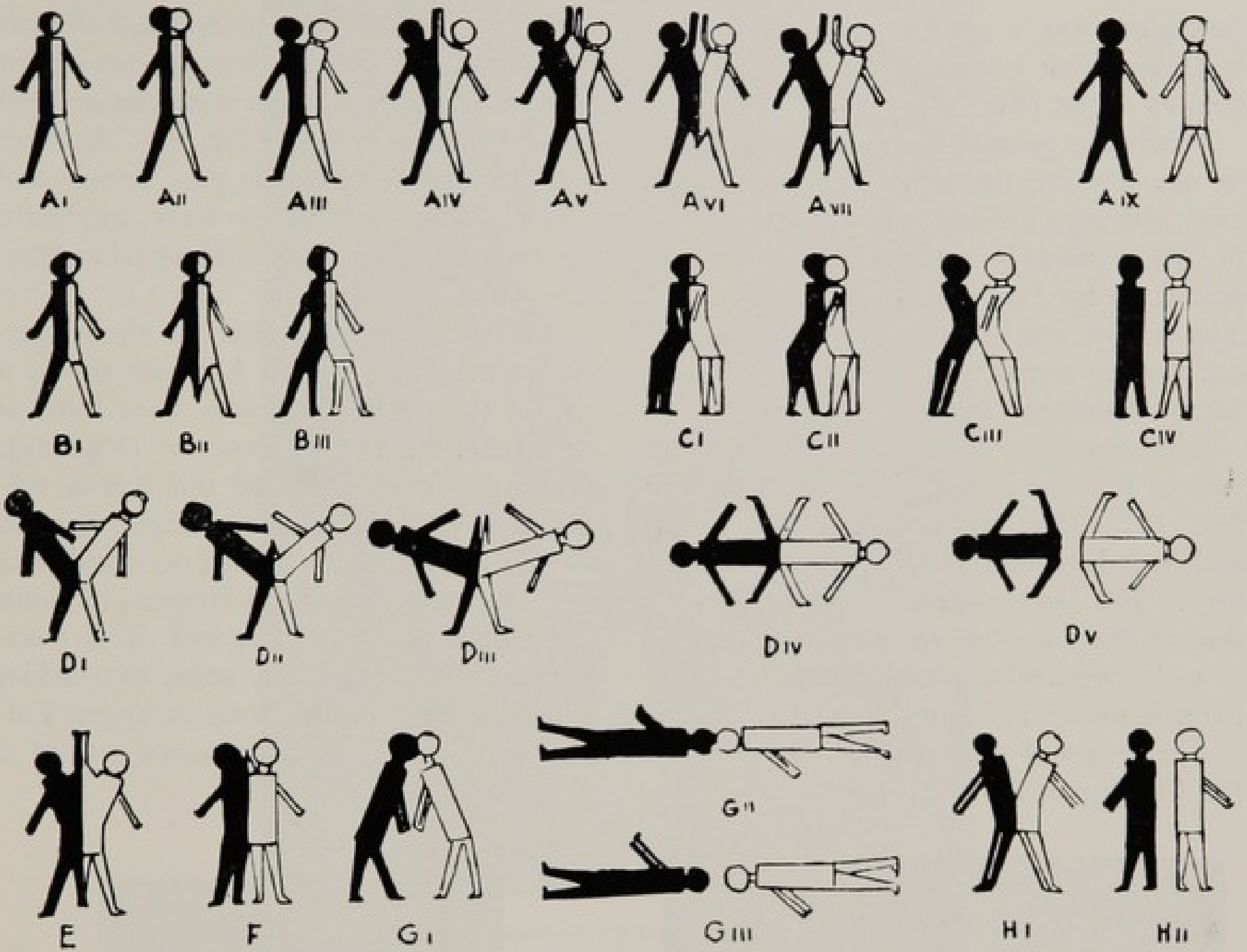


Fig. 64. Positional variations in symmetrical double formations, conjoined and separated (Schwalbe).

ganic fusion of the tissues (*Siamese twins*).

From a biological point of view, double monstrosities and Siamese twins represent misdeveloped uniovular twins in the same way that single malformations known to teratology are misdeveloped single individuals. It is not difficult to go from Siamese to identical twins, or trace similar twins to a single fertilized egg.

The connection between double malformations and twins is reinforced by the concurrence of both phenomena in certain families (Martin, Verey, Bohm, Dujol and Legros, Du Vernoi, Luksch and Ringelhan, Aschner and Gray). The gradual transition from some types of teratoma to MZ twins is shown in Table XXIX which summarizes double formations in man according to the classifications of Geoffroy Saint-Hilaire and Schwalbe. The positional variations in the uterus observed in symmetrical double formations (including one-egg twins) are schematized in Figure 64.

Obviously, the section of teratology dealing with double formations belongs to geminology or, more precisely, to the prenatal pathology of twinning. It may be of interest, therefore, to describe some of these human malformations. The group of asymmetrical double malformations includes the so-called *heteroadelphi*. Such a case was Lazzaro Colloredo, born in Genoa about 1625. Similar symptoms were observed by Monteau (1906) in a 13-year-old Indian boy who was presented at the Colonial Exhibition in Marseilles. Attached to this boy (autosite) was a parasitic cotwin without head but with crippled hands and a male urinary organ (Fig. 65).

When the parasite is located in a cavity of the autosite, the term *fetal inclusion* is used, although earlier writers spoke of *fetus in fetu* or *ovum in ovo*. Such a case was operated on by Lesi in the Faenza Hospital. The patient was 19 years old and presented a pararenal tumor which contained a perfectly structured fetus in miniature.

Representative of *teratoadelphi* was the case of Blanche Dumas, born in 1860 (Ahfeld, 1877). She had one head, one thorax and four legs, one of which was rudimentary. The genito-urinary orifices were double and so were the menstrual periods. A male pygomelus photographed by Williams is shown in Figure 66.

The group of *teratopagi* was represented by the xiphopagous Siamese pair, Chang and Eng (1811-1874), who traveled all over the world and became the prototype for all pairs of this kind who were thenceforth called "Siamese twins" (Fig. 67). Another example was the Canadian pair, Brenda and Beverly Townsend, who were surgically separated in the Edmonton Hospital in May, 1950 (Fig. 68).

An interesting bas-relief in the courtyard of the San Marco Museum shows a pair of male ischiopagi who were born in Florence in the 14th century (Fig. 69). Passerini (1853) described this pair as follows: "The historian, Buoninsegni, records the birth of a monster which occurred here in 1316 (that is, in the old Hospital of Santa Maria della Scala in Florence). This monster had two heads, four arms, two bellies and three legs. It was born in upper Valdarno and lived for 20 days, one part of it dying before the other. . . ."

Fig. 65. Autosite with anencephalic twin parasite (Monteux).

Fig. 66. Teratoadelphic pygomelus (Williams).

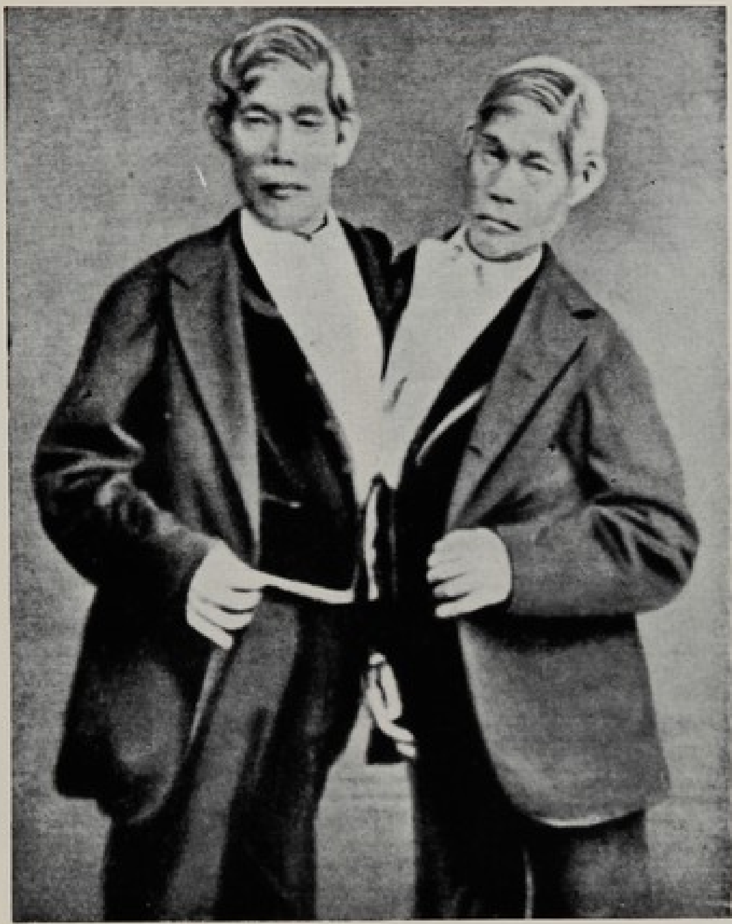


Fig. 67. The Siamese xiphopagi Chang and Eng.

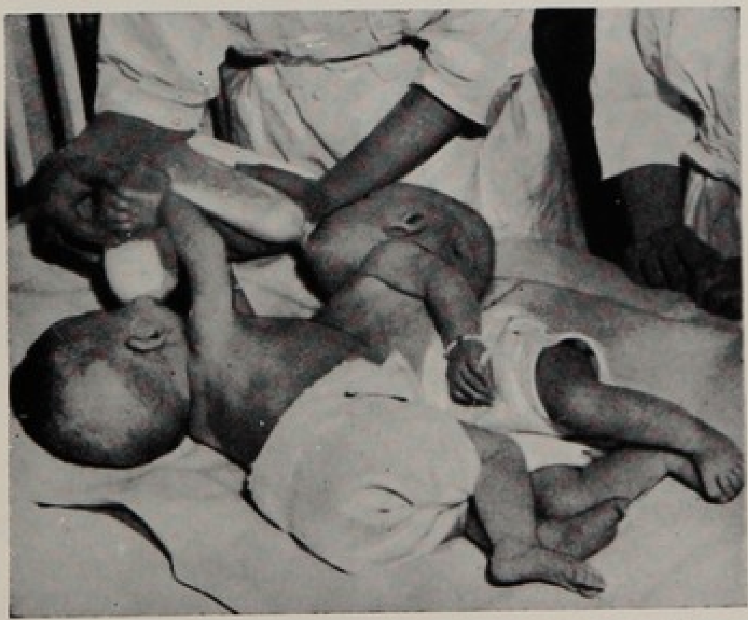


Fig. 68. The Canadian xiphopagi Brenda and Beverly Townsend at the age of five months.

Fig. 69. Male ischiopagi born in Florence in 1316 (Museum of San Marco).

Fig. 70. Female ischiopagi born in Portland, Maine in 1946.

A similar monstrosity or perhaps the same one was mentioned by Petrarch in his *De rebus memorandis*. A female ischiopagus was studied by Baudoin, and the birth of a similar case in Portland, Maine (Fig. 70) was reported by newspapers in 1946.

Of the many pygopagi recorded (lower dorsal conjunction), one of the earliest cases was that of two sisters who were born in Biddenden, England around 1100 and supposedly lived to 35 years of age. They were laterally conjoined in the gluteal and scapular regions (pygothoracopagi), each having one normal arm while both shared the stump of a third arm.

On October 26, 1701, the female pygopagi Helen and Judith were born in Szony, Hungary. At the age of ten years they were taken into the convent of St. Ursula in Pressburg, where they died on February 23, 1723. The case was fully described by Pope, Buffon and Torkos of the Royal Society of London. Werther (1707) mentioned the "Hungarian monster," too.

In 1873 the French Anthropological Society took an interest in the colored pygopagi Christine and Millie who were born in 1851 in a village in North Carolina. They were studied by Broca, Boens, Robin, Tardieu, Sangalli, Pancoast, Jackson, Rodriguez and De Parville. By the time they were 22 years old they spoke several languages. They both sang so well, Millie a contralto and Christine a soprano, that they were known as "the two-headed nightingale."

The Czech pygopagi Rosa and Josepha Blažek, born in 1878 and deceased in 1922, drew wide attention when Rosa gave birth to a normal child. From the start of her pregnancy not only her own breasts but those of her sister were enlarged, although up to eight weeks prior to Rosa's confinement Josepha continued menstruating. However, only Rosa felt fetal movements and had labor pains from uterine contractions. The discomfort caused by the dilatation of the external genitals was experienced by both sisters as they shared one vulva. Following childbirth, milk was produced by either twin, but in greater abundance by Rosa. Detailed anatomical descriptions were published by Perlstein and Le Count (1928), while Cummins (1936) reported on the fingerprints of this pair.

The problem of lactation was studied by Guttmacher in conjoined sisters who died in Chicago at 32 years of age in 1918. When one of them gave birth to a son, the other felt no pain, although both were able to suckle the child.

Well-known female pygopagi and performers were the Hilton twins, Daisy and

Fig. 71. The pygopagi Daisy and Violet Hilton (Lotze).

Violet (Fig. 71) born in 1911 and extensively examined by Bockenheimer (1911), Koch (1917), Newman (1931) and Cummins (1936), as well as the Gibb sisters (Fig. 72), reported by Cummins and Mairs (1934), Cummins (1936), and Ford-Walker (1952). Equally sensational were the Philippine pygopagi Lucio and Simplicio Godena who married twins and were skilled in a number of sports (Figs. 73 and 171). They were described by Van den Burg (1924) and Newman (1931).

Prominent among teratodymi is the case described minutely by St. Augustine as follows: "*Ante annos aliquot, nostra certa memoria in Oriente duplex homo natus est superioribus membris, inferioribus simplex; nam duo erant capita, duo pectora, quatuor manus, venter autem unus et pedes duo sicut uni hominis; et tamdiu vixit, ut multos ad eum videndum fama contraheret*" (*De Civitate Dei* XVI, 8). According to Phereponus, this case is identical with the double monstrosity mentioned by St. Jerome in a letter to the priest Vitale in the following words: "*Nostra aetate duplex Lyddae natus est homo, duorum capitum, quatuor manuum, uno ventre et duobus pedibus. . . .*"

Fig. 72. The pygopagi Mary and Margaret Gibb with their mother (Cummins and Mairs).

Fig. 73. The pygopagi Lucio and Simplicio Godena.

A historical pair of male xiphodymi lived at the Court of James IV, King of Scotland. They had two heads, two chests, four arms, one abdomen, two legs. They were accomplished linguists and musicians and lived to the age of 28 years.

A complete skeleton of teratodymi is preserved in the Medical Arts Museum of the Hospital of Santo Spirito in Rome. The skeleton is dated 1802, and a hitherto un-published photograph is reproduced in Figure 74.

The xiphodymi Ira and Galia were studied by Speranski, Anokhine and Alexéeva (1939) of the Russian Institute of Experimental Medicine and described as follows: "From an anatomical point of view, the exterior of these twins represents a single being with two heads and two pairs of small arms. From the shoulder region down their bodies form one trunk which ends in two small but normal legs. . . . The complete union begins along the upper thorax which has only two mammary glands. Only the interthoracic line of fusion, which is very prominent in the middle, serves to show that two babies contributed to the formation of a single thorax. There is only one

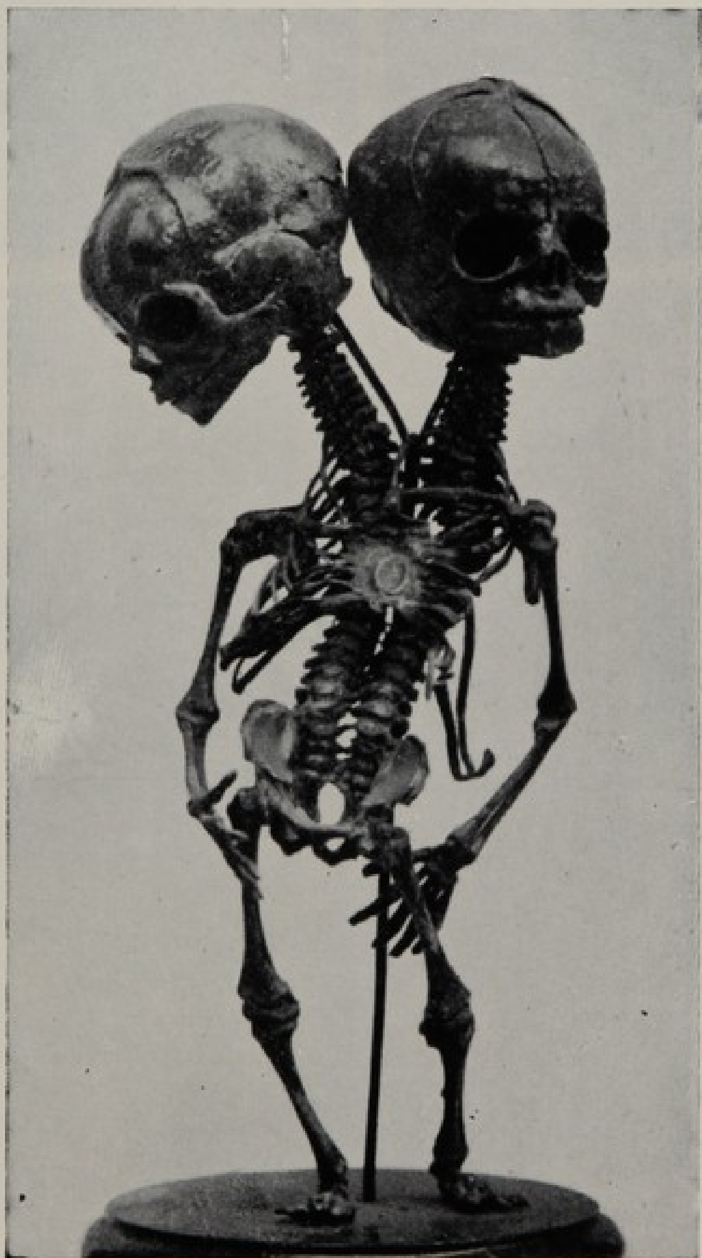
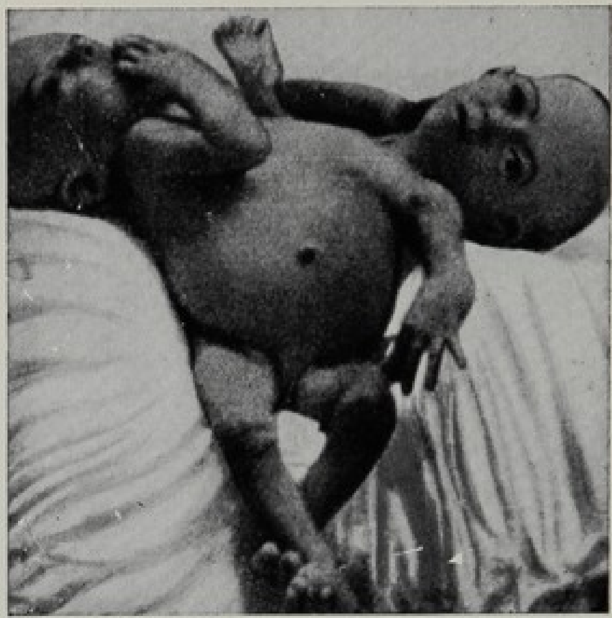
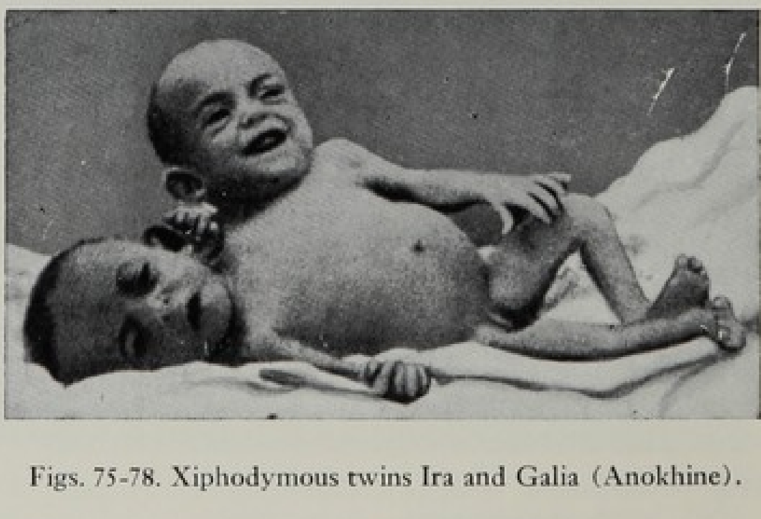


Fig. 74. Skeleton of teratodymi (Museum of the Hospital of Santo Spirito, Rome, 1802).





Figs. 75-78. Xiphodymous twins Ira and Galia (Anokhine).

umbilicus and all abdominal organs appear as if they belonged to a single child."

"Genital organs and anus," continue the authors, "are developed in the same way as in normal children. It seems that at birth each child, though sharing the same pelvis, possessed a separate anus, one of which was later closed. It may be assumed, therefore, that the two children have separate intestines. The coccyx ends in a small rudimentary tail. Roentgenographically, it can be seen that although there is only one simple body, two vertebral columns exist, running from head to pelvis and joining at the level of the coccyx. This fact is of particular physiological importance since it shows that the central nervous systems of the two children, from the brain to the spinal medulla, are entirely independent of each other. This arrangement makes it possible for the twins, to some extent, to receive individual nerve impulses. X-rays show that when food is taken by one mouth, it passes into the stomach belonging to the respective head. The same thing happens when the other head is involved. Therefore, each twin is able to nourish and satisfy herself independently.

"Electrocardiographically, it can be seen that the twins have their own hearts with a non-synchronous pulse. Each heart follows its own rhythm and reacts in its own way to external stimuli. The reactions and attitudes of the girls towards the outer world are distinguishable from each other to the degree that either Galia or Ira smiles when her name is spoken. The last photograph shows them at a moment when Ira is smiling, while Galia rests quietly. . . ." At the age of one year, this pair died of pulmonary complications (Figs. 75-78).

Among symmetrical double malformations, one finds *craniopagi* conjoined in the upper part of the cranium. Typical examples were the Stoll twins, born in Frankfurt in 1922 and examined in Berlin, as well as the Smith twins who were born in Wyn-

Fig. 79. Craniopagous twin sisters Kathleen and Lexie Smith, born in Wyñyard, (Tasmania) in 1950.

yard, Tasmania, in 1950 (Fig. 79).

Our understanding of double malformations is increased by Dondero's x-rays (1937) of cephalothoracopagous deradelphi (Fig. 80), and of an asymmetrical double formation called epignathus, where the parasite is attached to the palate of the autosite (Fig. 81). Also reproduced are the photographs of a teratodymus (Fig. 82), heterodymus (Fig. 83), and sternoxiphopagus (Figs. 84 and 85) provided by Boni and De Camillis (1949). The last case is particularly interesting since the thyroid glands of the twins are enlarged and injection of a radiopaque substance reveals a large artery branching out from the abdominal aorta and connecting the two circulatory systems.

As to the multiplicity of malformations observed in twin teratology, one may well remark that truth is stranger than fiction. There are so many possible combinations here that no matter how elaborate our system of classification, it will at times prove inadequate and limited in value.

Although Lotze believed that "MZ twins are no more than a malformation to which fortune has been kind," it cannot be said that the principal phenomenon is represented by the malformation. Actually, the basic process is that of a gemination brought about by a hereditary predisposition. From a biological standpoint, then, it would be more appropriate to reverse the phrase and say that double malformations are no more than a case of twins to whom fortune has been unkind.

Fig. 80. Cephalothoracopagous deradelphi (Institute of Pathological Anatomy, Pavia).

Fig. 81. Epignathus with the parasite attached to the palate of the autosite (Institute of Pathological Anatomy, Pavia) (Dondero).

Fig. 82. Teratodymus (Institute of Anatomy, Rome).

Fig. 83. Heterodymus (Institute of Anatomy, Rome).

An important feature of double malformations was noted by Geoffroy de Saint-Hilaire; namely, that the union always takes place between homologous parts. This fusion of homologous parts was assumed to be the result of what French authors called the law "d'affinité de soi pour soi." Dareste and Apert believed that, with embryos developing side by side, homologous parts of each organism were bound to be found at the same level.

In our opinion the situation is rather different, i.e. the given process is not a secondary step toward conjunction, but a failure of two primordial embryos to separate. In any case, the phenomenon is a very interesting one and casts some light on the mechanism operating in diplogenesis. Further, it proves that the positions of MZ fetuses in the uterus, where homologous parts do not correspond, are a secondary effect not of diplogenesis but of subsequent mechanical influences.

In closing, another fact observed by Geoffroy Saint-Hilaire may be mentioned; namely, that double malformations are more frequent in the female than in the male. In a series of 355 double malformations, Forster found 232 female and 123 male cases (2:1). When symmetrical and asymmetrical malformations were separated, the sex ratio was 209 females to 76 males in the former group (3:1) and 23 females to 47 males in the latter (1:2). In Apert's opinion, "*La raison de ces prédominances nous échappe*," and it is evident that these statistics need confirmation.

Etiologically, there is little doubt that double malformations arise from a delayed and incomplete division of a twin embryo

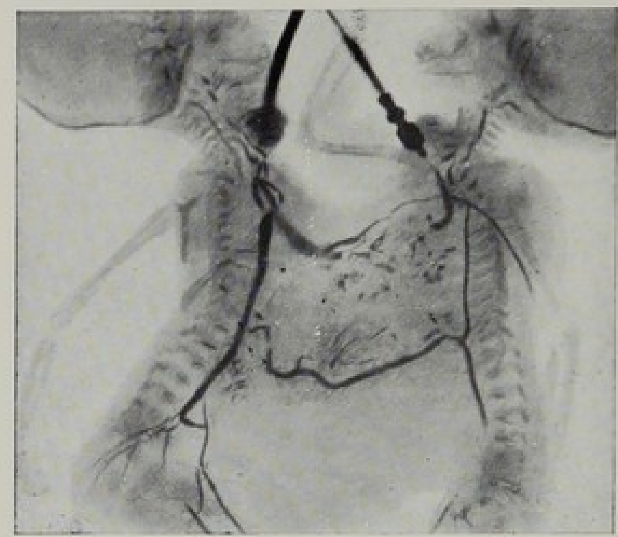


Fig. 84 (Left). Sternoxiphopagus (Obstetric Clinic, Rome). Fig. 85 (Right). Arteriogram showing a common carotis and an abdominal anastomosis (Boni and De Camillis).

at the time when only one system of membranes has been formed. Therefore, such twins have only one placenta, one chorion, one amnion and one umbilical cord. In view of this fact, some authors were inclined to stress the similarity between nonseparated double formations (double malformations) and separate ones (uniovular twins), suggesting the name *chorionangiopagi* for the latter (having only one chorion and one placenta). However, the term would seem inappropriate not only because some MZ twins have two chorions and even two placentae, but also because there is no reason for extending the concept of embryonic conjunction to the membranes.

EMBRYOGENESIS OF MONOZYGOTIC TWINS

Historically, it may be of interest to recall the theory of Broman (1902) that atypical giant spermatozoa, or spermatozoa with two heads or two tails, attributed to alcoholism or syphilis, might cause the formation of two organization centers in a single egg. According to Broman, the proportion of spermatozoa with two tails varies between 1 and 40% in man. The same idea that two-headed spermatozoa determine gemellogenesis was held by Hoeffer (1909). The implausibility of this theory, however, is demonstrated by the fact that in this way the gemellogenetic factor would depend only on the father, and there would be no explanation for its transmission on the mother's side.

Sobotta rejected the theory on the grounds that in the case of the armadillo one would have to assume the improbable occurrence of spermatozoa with 12 tails. It may be mentioned, however, that Deluca and Widakowich (1919) found double-tailed spermatozoa in 6 out of 1,000 healthy persons, in 13 out of 1,000 syphilitics, and in 32 out of 1,000 congenital syphilitics. This increase of two-headed spermatozoa in syphilitics was assumed to be responsible for a higher frequency of twins among such persons. However, as syphilis can be ruled out as a cause of twinning, Dahlberg was correct in concluding from these findings that atypical spermatozoa play no part in gemellogenesis.

Various other theories have at best a historical value. It was suggested, for instance, that identical twins are derived from two fused eggs. Based on experiments with eggs of echinoderms and worms, the theory implied that the fusion of two eggs into one single giant egg would give rise to two more or less separate individuals, or even single individuals. Another theory postulated that identical twins may originate from more than one egg contained in the same follicle, or from binucleated eggs. Of course, all these theories are incompatible with the principles of modern genetics, and it is now generally accepted that identical twins are derived from a single fertilized egg. The pertinent question here is, how and when during the process of ontogenesis does this doubling take place?

In line with experimental data obtained by Spemann and others through artificial strangulation of the fertilized egg, the onset of diplogenesis may be assumed to occur in a very early period of development. As it would be difficult to conceive of an intervention by some external factor comparable to those used in the experiments, endogenous factors have to be considered. Hence we may accept Poyer's observation (1921) that gemellogenesis may in fact be compared with the division of the protozoa, where no factor outside the individual itself has any part in the phenomenon of reproduction.

However, Spemann, by means of experiments with the fertilized egg, was able to produce only proportionately under-developed individuals, thus differentiating this process from that which normally occurs in man. While MZ twins may be underweight at birth, they always exceed one-half the weight of the average single-born and in postnatal development usually reach a normal weight level, showing no signs of microsomia in comparison with their parents.

Another theory was based on the assumption of an ontogenetic process taking place during the phase known as "stage of two blastomeres." That uniovular twins might originate in this very early stage of ontogenesis was hypothesized by Chiarugi (1926) in view of his observation of the occurrence of two six-week-old biamniotic monochorionic human embryos. The two blastomeres were assumed to develop in such a way as to give rise to two embryos, although failing to separate completely. With two morulae having been formed by the segmentation of each blastomere, they would continue their development in mutual contact. A cellular mass giving rise to the embryonic nodule would become differentiated in each of them, the peripheral part representing the future trophoblast, to be formed only along the free surface of the two embryos and not within the line of contact. This explanation would be in line with the theory that the evolution of embryonic cells essentially depends on their position.

Deviating from the usual pattern of evolution, the septum between the two blastodermic vesicles might easily be destroyed by their expansion, thus allowing the two amnions to come into direct contact. Indeed, the particular situation of the membranes observed by Chiarugi in the given case, as well as the fact that the chorion seemed to be asymmetrically divided into two segments, led him to believe that everything was in favor of an early fusion between two separate blastodermic vesicles, rather than a particular evolution of a primitively simple and regularly spheroid blastodermic vesicle. Upon further development, traces of the duplication of the chorionic vesicle might become unrecognizable. In effect, this process would result in *secondary monochorionics*.

According to v. Verschuer (1933), too, gemellogenesis may originate from the division of the first cells of segmentation with a doubling of both the embryoblast and the trophoblast, thus producing a double chorion derived from the trophoblast. Subsequently, the two embryonic units may remain more or less in contact, so that their implantation in the uterine mucous membrane may be single or double. It would follow that the placenta may also be single or double.

The assumption that twinning in man begins when the egg is at the stage of two blastomeres was criticized by Levi (1922). It was claimed by him that in human ova and those of all mammals, the presence of the secondary egg membrane would prevent even a partial separation of the two blastomeres. Moreover, the ability of the two blastomeres to form complete embryos had been demonstrated only in invertebrates and anamniotic vertebrates in which the constitution of the egg, and therefore the first stages of development, are entirely different from those in mammals and man. Finally, no case was known of spontaneous isolation of the blastomeres in anamniotic organisms.

Since it was thought at one time that all twins and double malformations were due to an accidental separation of the first two blastomeres, Morgan (1938) emphasized the resemblance between the division of eggs of small mammals into two, four, eight or more blastomeres and the segmentation observed in *Amphioxi* and *Echinoderms*. In his opinion, however, this resemblance is only a superficial one, since no duplication occurs in the early stages.

Dalcq (1939) was as skeptical as Sobotta regarding the possibility of explaining the genesis of human twins and double malformations by the existence of eggs with the capacity of rearranging the contents of the first blastomeres (in such a way as to make them equally potent). He pointed out that a division at the stage of two blastomeres would lead to the formation of two independent systems of fetal membranes, while generally both the placenta and chorion are single. His conclusion was that whatever interest we may find in knowing that each blastomere may give a complete egg, this does not explain what happens when the anomaly is spontaneous.

In the case of a single conception, the blastomeric stage is followed by those of the blastosphere and the blastodermic vesicle (blastocyst). Here a cavity is seen in the product of conception (future cavity of the chorion) and two entities are noted: the trophoblast or membrane from which the chorion is derived, and the embryoblast from which the embryo proper develops.

It is this phase of ontogenesis to which most investigators have attempted to trace the onset of uniovular twinning in man. Some authors, such as Zietschmann (1931), doubt that this type of gemellogenesis is possible before the period of the primitive node or blastocyst. Instead, they attribute the occasional occurrence of dichorial uniovular pairs (mentioned in connection with gemellogenesis in the stage of two blastomeres) to a secondary division of the chorion.

The tendency to attach so much importance to the period of the blastocyst is motivated by certain observations in sheep and pigs, and chiefly by known gemellogenetic events in the armadillo. These findings have been described before (see Chapter III), but the various ways in which this phenomenon is assumed to occur in human twinning will be discussed here.

As human ova attach themselves to the uterine wall at an earlier developmental stage than is true in the armadillo, the subdivision of the ectoderm (the presumable cause of the duplication) may take place after the implantation of the ovum in the uterine wall (Levi). Apparently, the development of "Streeter's ovum," described in 1919, falls at the end of the second week, a circumstance yielding important evidence for the theory that the two embryos separate long before the appearance of the primitive streak (as in the armadillo), and probably before the formation of the amniotic cavity (in contrast to the armadillo).

Two hypothetical schemes (A and B) are provided by Streeter to explain his histological finding (C) in Figure 86. The larger twin embryo is seen with its membranes, while the cotwin, whose amniotic cavity is detached from the yolk sac, reveals an early arrest of development. The surviving embryo is 0.92 mm. long, but the amniotic cavity and yolk sac of the rudimentary twin partner measure only 0.1 mm. and 0.03 mm. in diameter, respectively.

Hence it may be assumed that the internal cellular mass of the blastocyst, which normally forms the only embryoblast, divides itself into two masses from which, at the end of the process, two embryoblasts are derived. If the division is equal and complete and the respective embryoblasts fully separated from each other, the embryonic areas into which they are transformed will be unconnected, each one developing by itself. Both embryonic areas give rise to a normal embryo which has its own amnion and yolk sac, that is, those particularly essential membranes connected directly with the body of the embryo. It is the trophoblast, which normally contains the blastocyst, that serves as a foundation for the development of the single chorion (Chiarugi).

According to this theory, the division of the embryoblast leads to the formation of uniovular biamniotic monochorionic twins. As the amnion is still unformed at this stage of development, the two embryoblasts develop separate amnions later on. However, there will be only a single chorion, since the differentiation of embryoblast and trophoblast (the chorion being derived from the latter) takes place before the division (v. Verschuer).

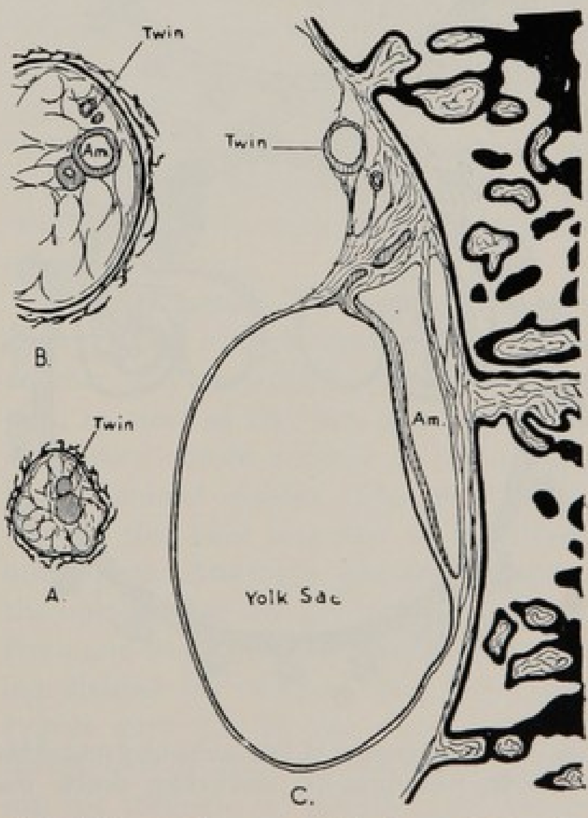


Fig. 86. Streeter's ovum (C) in human MZ twinning (Droogleever Fortuyn).

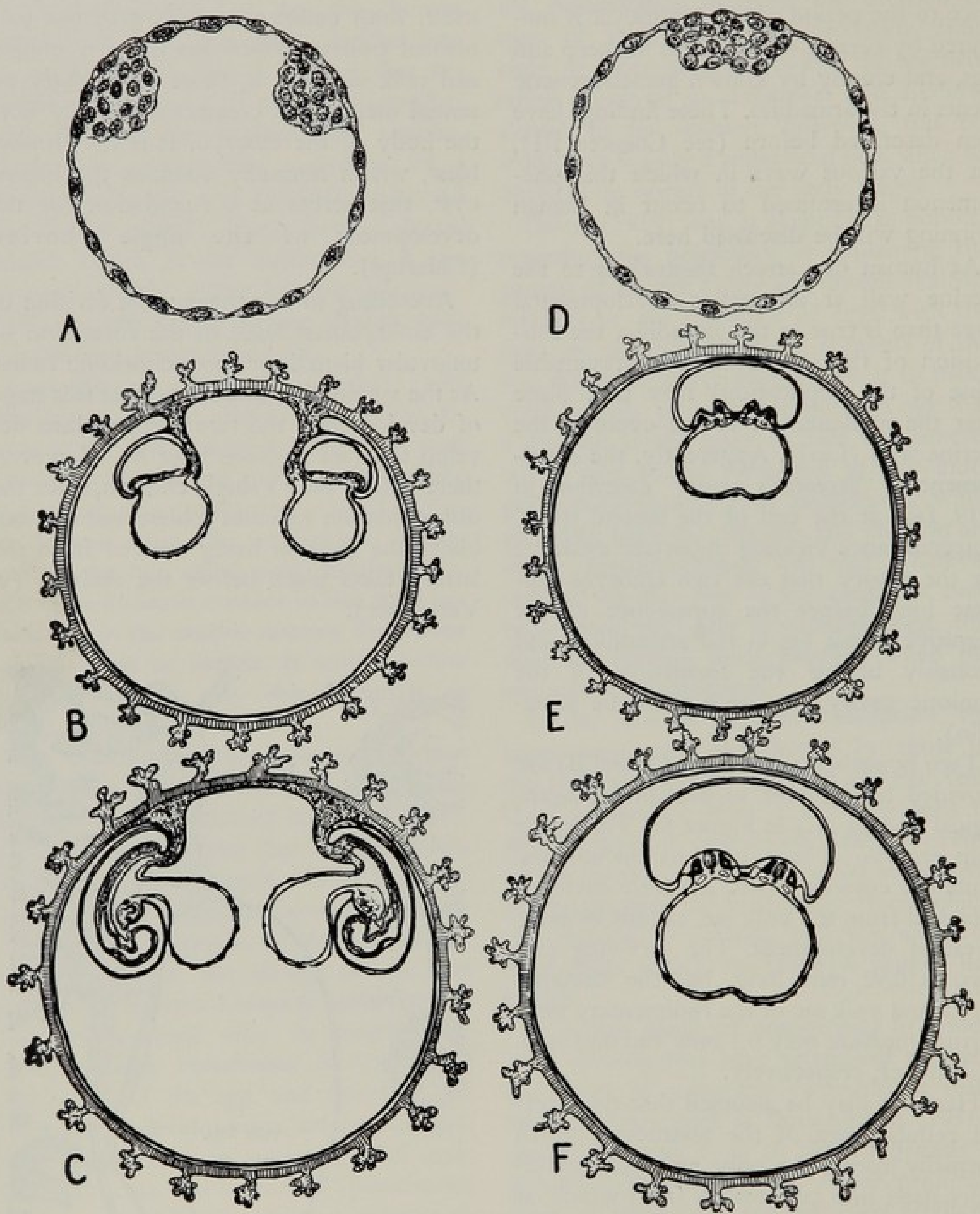


Fig. 87. Development of two uniovular monochorionic biamniotic twins (A, B, C), and of a monochorionic monoamniotic univitelline double malformation (D, E, F) from a single egg (Patten).

The given mechanism is schematically explained in Figure 87. Depending on whether the cellular mass of the blastocyst is divided completely or incompletely, either a set of uniovular biamniotic monochorionic twins (A, B, C) originates, or a double malformation (D, E, F).

In the last analysis gemellogenesis in the armadillo, as described by Patterson, Newman and Fernandez, constitutes the most conclusive evidence for a similar process in man. It is a spontaneous phenomenon, unlike those artificially produced in experimental embryology, and fully compatible with what is known about embryonic twin structures in the human species.

Therefore, Aron and Grassé (1939) were probably correct in stating that true human twins derive from the same ovum and the placenta is single, while the membranes are generally double. Nothing is known of the first stages of these embryos. Perhaps they derive from proliferating zones, such as those of the Tatusia (armadilli) where they separately originate from the wall of the primitive embryonic formation.

Ontogenetically, it is a fact that the stages of the embryonic area and primitive line follow that of the blastocyst. According to some authors, this period may also become the starting point for uniovular twinning. For example, duplication of the embryonic area and primitive line has been assumed by v. Verschuer to be capable of leading to the production of uniovular monoamniotic and monochorionic twins. In this period, with the differentiation of both chorion and amnion having already taken place, these membranes are beyond the possibility of duplication. In the opinion of Lotze, too, twinning may take place in the early stage of the embryonic area and primitive line. If it occurs later, it may no longer result in the formation of separate twins.

It has been claimed, therefore, that uniovular twins formed within a common amnion are genetically close to double malformations. This theory received support from Steiner's observation of only one malformation in a series of 24 uniovular dichorial pairs, as against three malformations in 32 uniovular monochorionic biamniotic pairs, and one malformation in three monochorionic and monoamniotic pairs. It would seem, therefore, that when gemellogenesis begins later malformations occur more frequently.

According to Dalcq (1939), the turning point of diplogenesis lies in the production of more than one primitive line. Modern embryological data imply that the formation of the primitive line is not due to a local cellular proliferation, but to a mass movement of all the cells included in the embryogenic zone, thus giving the primitive line the same significance the blastopore has in lower animals (Pasteels). Any anomaly in these movements determined, for example, by the manifestation of two converging foci (Graeper), may be able to produce the phenomenon of diplogenesis, resulting either in twins or in double malformations (Dalcq).

The mechanism by which MZ twins emerge from a single ovum in one way or another may actually be even more complex, in view of the fact that higher multiples may consist entirely of MZ twins in higher animal species. The most famous case of this kind was that of the Dionne quintuplets. American geneticists were of the opinion that the five girls were derived from one ovum in the following way: Having divided for the first time, the original zygote gave rise to two totally potential halves. One of them divided again, producing the embryos of Annette and Yvonne. Division of the other half produced Cécilie, as well as a fraction which, again splitting into two, gave rise to the embryos of Marie and Emilie (Fig. 88). This explanation was supported by the fact that Marie and Emilie showed evidence of reversed asymmetry (for example, Emilie was the only left-handed girl of the set) and also by the relative degrees of resemblance which in decreasing order were as follows: Emilie, Marie, Cécilie, Yvonne, Annette (MacArthur, 1938).

Commenting on the birth of these MZ quintuplets, Dafoe (1934) disclosed that at the beginning of the third month of pregnancy, the mother complained for two hours about pains similar to labor pains, "after which she emitted a black ovoid object from the vagina of about the size of a duck's egg."

MacArthur and Ford (1937) assumed this was the abortion of a sixth embryo. They disproved the common belief according to which, as cell divisions do not produce odd numbers, the Dionne set should have consisted of six members. Although the sixth embryo possibly existed, the production of six fetuses does *not* indicate a symmetrical division which would originate *eight* fetuses. Asymmetry being thus involved in the production of either five or six embryos, the former may be accounted for as easily as the latter. The occurrence and relative frequency of identical triplet, quadruplet and quintuplet births is proof that the process of identical twinning does not necessarily produce either odd or even numbers.

Passing mention may be made here of a rather academic notion regarding one-egg twinning. Since MZ twins are derived from a single zygote which later divides into two

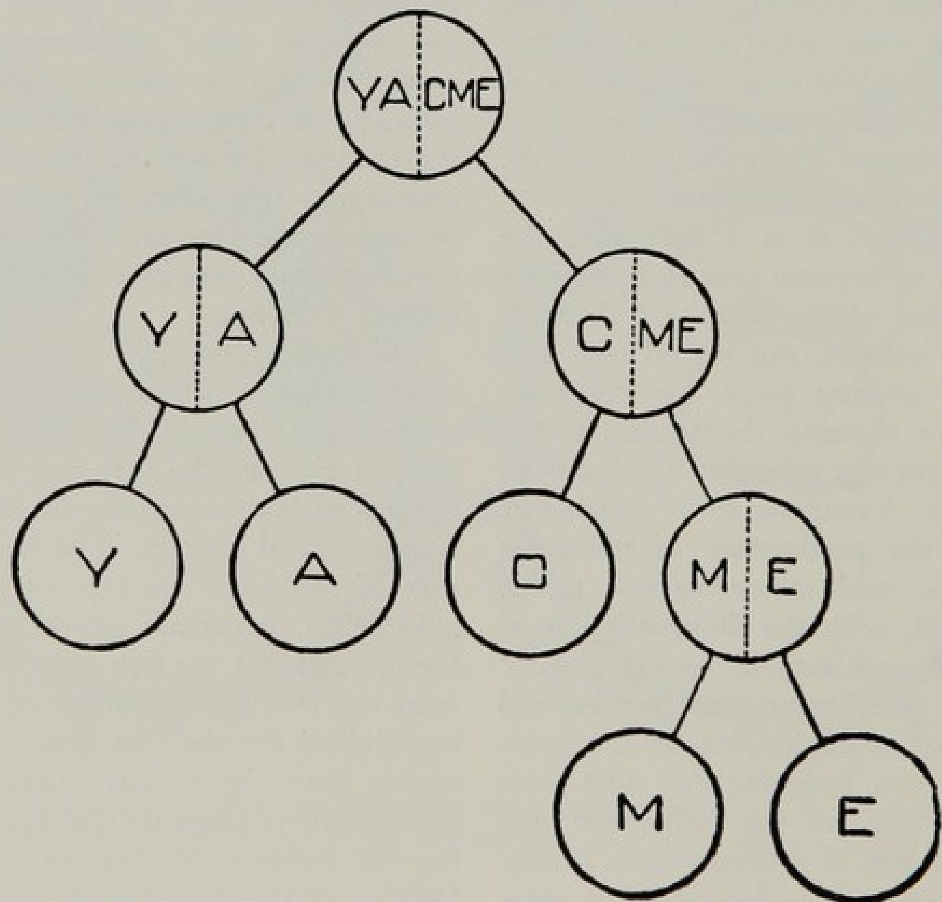


Fig. 88. Uniovular embryogenesis of the Dionne quintuplets, Yvonne, Annette, Cecilie, Marie, Emilie.

identical ones, some biologists have raised a somewhat perplexing question. Would it not, they ask, be correct to say that the single zygote represents the son, while the twins derived from its division technically are the sons of the son or the grandchildren of what apparently is the mother but actually is the grandmother? Obviously, this conjecture is the result of splitting hairs, and should serve to remind us that in science, too, that ancient proverb, *summum ius, summa iniuria*, applies.

EMBRYOGENESIS OF PLURIZYGOTIC TWINS

In considering the alternative of dissimilar twins from an embryological point of view, we are mindful of the fact that this subject has to be approached differently in that such twins show significant biological differences in sex, blood groups, color of the hair and iris, and the like.

As to the embryogenetic mechanism responsible for this type of twins, the customary explanation is that dissimilar twins originate from two different ova which reach maturity and fertilizability at the same time and are fertilized by two different spermatozoa. Thus the two individuals produced, except for their simultaneous conception and delivery, may be compared to the zygotes of two brothers born at different times. Weinberg was the first to offer this explanation and, later, many other authors followed suit.

Therefore, it is said that similar twins are produced by pluriembryony and dissimilar ones by pluriovulation. The pluriovular theory of the origin of dissimilar twins is based largely on the fact that animals producing multiple fetuses show a simultaneous eruption of several oophorous follicles with fertilization of the respective ova (Fig. 89). Under exceptional circumstances, the hu-

Fig. 89. Rabbit ovary with numerous hemorrhagic areas from the simultaneous eruption of a corresponding number of oophorous follicles (observation of Gedda and Maltarello following Friedmann's pregnancy test).

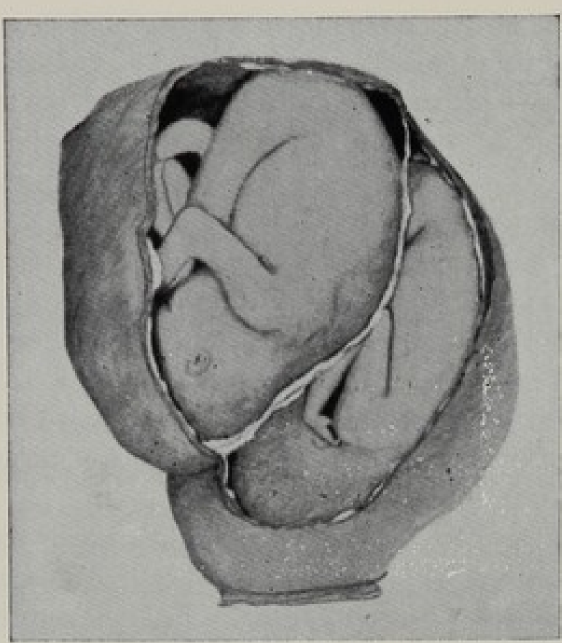


Fig. 90. Opposite-sex DZ twin pregnancy.

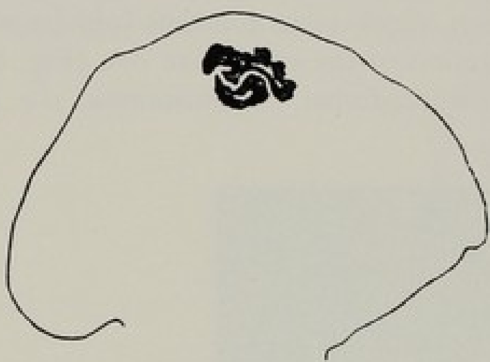


Fig. 91. Corresponding right ovary with two corpora lutea (Cummins).

man ovary is also known to produce two or more oophorous follicles at the same stage of development, or two or more corpora lutea released by the same number of ova. In twin pregnancies two corpora lutea were found in the same ovary (Dahlberg 1926).

Allen (1930) observed in a collection of fertilized human ova that there was one case with an ovum in each Fallopian tube and with a corpus luteum in each ovary. Another interesting case was that of a primipara reported by Essen-Möller (1936) with a surgically removed pregnant uterus and a large corpus luteum in each ovary. When the uterus was opened, two dichorial embryos were found. Likewise, Cummins (1942) described a removed uterus containing a dichorial opposite-sex twin pregnancy approximately at the eighth month stage. Histological examination revealed two closely attached corpora lutea in the right ovary, and no corpus luteum in the left ovary (Figs. 90 and 91).

While there is no doubt that pluriovulation may result in the production of dizygotic twins, it is not so certain that this is the only mechanism whereby dizygotic twinning takes place. Obviously, only the transmission of the phenomenon on the mother's side can be explained in this way, but the inheritance of a factor for two-egg twinning on the father's side remains unexplained. With pluriovulation the *conditio sine qua non*, and a strictly female prerogative, how can the father transmit the tendency to two-egg twinning if the mother does not cooperate with the simultaneous maturation of more than one ovum?

This question remains veiled in obscurity even in the face of some of the other theories of dizygotic twinning which have been proposed without, however, gaining much popularity. One of them attaches particular significance to the fact that pluriovular follicles occur in the female ovary.

In a patient who had a fatal hemorrhage during a twin pregnancy, Bumm found two or three ova in each follicle. So did Rabl (1899) and Strassmann (1904), the former discovering fairly mature follicles with several ova in a 25-year-old multipara, as well as Häggström (1921) who described atresic follicles with different ova in a young multipara (age 21) that he interpreted as the result of a degenerative parthenogenetic process.

Similarly, Wieman and Weichert (1936) mentioned autopsy findings of a uterus which contained dichorial twins of the same sex, accompanied only by one corpus luteum in the ovaries. However, with no conclusive zygosity diagnosis in this case, it is unclear whether the twins were dizygotic but came from a single biovular follicle or monozygotic with a double chorion.

At this point, a hypothesis proposed by Lenz may be described. While also based on biovulation, it follows an entirely different pattern of reasoning. According to Lenz, pluriovulation in women is rather frequent, but usually does not result in the conception of twins. Ordinarily, when an ovum is fertilized, some unidentified inhibitive substances are supposedly formed, preventing the fertilization of other ova. Thus mothers of dissimilar twins would simply be women in whom this inhibitive mechanism had failed.

Lenz believed that "the simultaneous maturation of different ova is not the essential cause of twin births." In his opinion, other experiments show that the simultaneous elimination of several ova is much more frequent than the birth of twins. As a rule, following impregnation of an ovum in the uterus, substances are formed which prevent the fecundation of other egg cells. A deficiency in the production of these substances, either on the maternal or on the paternal side, would favor the generation of twins. Apparently, it is assumed that the father may also be responsible for the nonproduction of inhibitive substances. It seems, therefore, that the production of such substances is thought to be a special function of the male and female gametes which unite in the zygote.

Another situation, less common, may also produce dissimilar twins. Obviously, fertilization is doubled when it depends on two different men. This event is known as *superfecundation* and gives rise to twins who are only half-brothers, although sharing the same uterus. Instances of superfecundation have been described in such animals as cows (Fig. 27) and dogs. In the latter, mating during estrus with dogs of different breeds results in various bastard combinations. Similarly, mares mated with a horse and a donkey may give birth to twins one of which is a horse and the other a mule. In humans, instances have been reported of white women who had intercourse with a white and a nonwhite man and gave birth to twins each of whom showed different racial characteristics. Similarly, a pair of twins with one Negro and one mulatto member was born to a Negress (Archer, 1809).

Referring to Andreassi's studies (1947), Clara mentioned the case of a biovular pregnancy in a married woman who also had intercourse with a man other than her own husband. Examination of the blood groups of the two infants (a male and a female) showed that they could not have been conceived by the same father. Apparently, the boy was from the husband and the girl from the lover. Actually, some authors speak of superfecundation when the second twin is conceived by the same man but at a later time. In any case, superfecundation refers to ova synchronously produced and released.

In this connection, mention should be made of the phenomenon of *superfetation*. Although denied by many authors, it may occur when the conception of a first individual does not interfere with the implantation of further ova (normally affected by the hormones of the corpus luteum). Another ovulation would make it possible for a pregnant woman to conceive a second child either from the same or some other man. If these men should be of different races, superfetation would give rise to racially different twins (De Bouillon, 1820).

Certainly, the theory of pluriovular follicles, as well as those of superfecundation and superfetation, is compatible with the concept of biovular gemellogenesis. Another hypothesis, formulated by Stöckel (1894) and Rabl (1899), based on the cytologically verified occurrence of binucleated eggs, has received little attention. Its implication is that there are twins who are genetically dissimilar, although they are derived from a single (binucleated) egg. Apart from the theory of pluriovulation, however, the most plausible explanation of dissimilar twins is the one based on the concept of "oocytic twins."

Of particular importance in this respect are Sobotta's observations (1914) on the maturation and fertilization of ova in warm-blooded animals, such as the mouse. In vertebrates, it seems that the spermatozoon penetrates the female gamete before the second maturation division, i.e. before the expulsion of the second polar body. Sobotta pointed out that, as known from exact studies on the expulsion of the second polar body, this does not take place without fecundation. If the egg cell is not fertilized, it perishes together with the second polar body.

This observation led Sobotta to formulate the following important theory: the polar bodies are not only well formed cells, but are actually mature germinal cells with the number of chromosomes reduced. It is possible, therefore, that even polar bodies may sometimes be fertilized. In other words, he was inclined to believe that polar bodies may sometimes have the same significance as authentic female gametes capable of fertilization.

Lindahl (1937) also described this type of twinning in the *Arbacia pustulosa*. In some females, he found ova with unusually large centrosomes. The volume of the two cells formed was the same as that of a normal oocyte, and even the two nuclei corresponded to the size of ordinary nuclei. The gelatinous covering membrane was shared, so that only one micropyle was found. It was suggested that these double ova may be fertilized and result in the formation of separate blastocysts.

As previously mentioned, Danforth (1916) applied these ideas to two-egg twinning in man when he studied the frequency of this phenomenon in 50 St. Louis families. Referring to Boveri's experimental work in this area, he postulated the existence of a third type of twins, assuming that the two cells produced by the division of the secondary oocyte may be fertilized by separate spermatozoa.

Similar views were expressed by Fisher (1919), but on an entirely different basis. As the result of a statistical analysis of Thorndike's twin data, the British expert suggested a third group of twins, whose intra-pair resemblance, although less pronounced than that of MZ pairs, would be expected to consistently exceed that of DZ twins and ordinary sibs. The degree of resemblance characteristic of this third group would be of the same order as could be predicted if the twins were to divide the hereditary material of one gamete, but not of the other. This condition would be met if, after maturation, the ovule could be induced to divide into two identical portions which, in turn, could be fertilized by different spermatozoa.

Curtius' theory (1927) was similar to that of Sobotta and also based on studies in mice. With fertilization being an indispensable process for the emission of the second polar body in cold-blooded animals (*Amphioxux*, *Petromyzon*, *Amphibians*), as well as in warm-blooded ones (mice), the same mechanism was assumed to be necessary in man. In mature ascidian eggs, the polar bodies are not emitted before fertilization is completed (Morgan, 1895). Similarly, in the elongated eggs of insects, which are covered with a hard layer and fertilized by spermatozoa contained in the seminal vesicle, the emission of the polar bodies occurs only after impregnation.

Following a careful examination of Sobotta's cytological material, Curtius was convinced that "because of the high degree of quantitative and qualitative development of the polar body among mammals," this structure might also be capable of fertilization under the influence of a dividing factor, acting at a time when division is possible, i.e. before the separation of the second polar body

This dividing factor, termed the G factor or gemellogenetic factor, would conceivably be able to act when brought into amphimixis by the mother or the father. In either case, its action would determine the emission of a second polar body capable of fertilization. Later, when another spermatozoon succeeds in fertilizing the second polar body, it would lead to the simultaneous presence of two zygotes, one produced by the secondary oocyte being fertilized by the first spermatozoon, the other by the second polar body being fertilized by the second spermatozoon.

The two zygotes thus produced will be genetically dissimilar. Such twins may be called dizygotic, but cannot be regarded as biovular since they are derived from a single ovum rather than two different ones. Arising from the two polar bodies after separation from the same ovum during the second division of maturation, these twins are uniovular although differing in their genotypes (Fig. 92).

Fig. 92. DZ twins derived from one ovum.

In line with Curtius' hypothesis, it is easy to understand that the action of the G factor is established in the first zygote where it determines the emission of a polar body capable of fertilization. As a rule, it does not influence the second zygote, since both polar body and spermatozoon have different chromosomes. In the case of maternal inheritance, the polar body cannot contain the G factor, known to belong to the egg cell and to have fulfilled its function on the first zygote with the production of a polar body capable of being fertilized. In the case of paternal inheritance, the laws of probability also make it very difficult if not impossible in practice for the second spermatozoon to carry the G factor. Consequently, the process of twinning usually stops at the implantation of two zygotes. However, this theory would also explain why higher multiple sets may be composed of similar and dissimilar twins.

As mentioned in the preceding chapter, Curtius was inclined to believe that the hereditary factor for twinning is single-factorial. In other words, the G factor may determine the formation of both similar and dissimilar twins. If it is carried by the father as well as the mother, it cannot be expected to be possessed by all egg cells and spermatozoa. Where the egg cell carries the G factor, it will determine the emission of a fertilizable polar body, while the spermatozoon does not contain the G factor. However, where the father also carries the trait, a second spermatozoon with the G factor may fertilize the polar body, giving rise to a process of gemellogenesis. This process cannot repeat the production of another polar body, but will result in the ordinary phenomenon of one-egg twinning. As a result, two similar MZ twins with a dissimilar partner will be found in

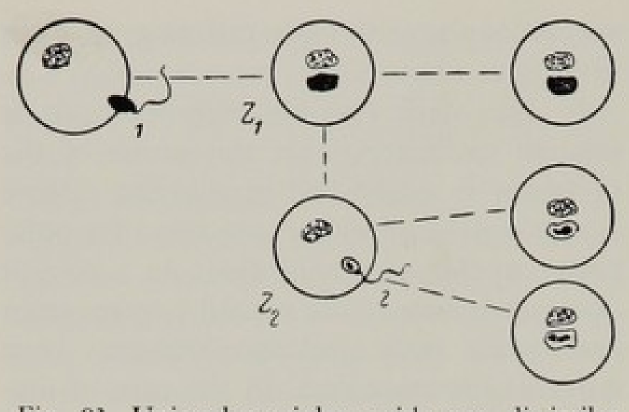


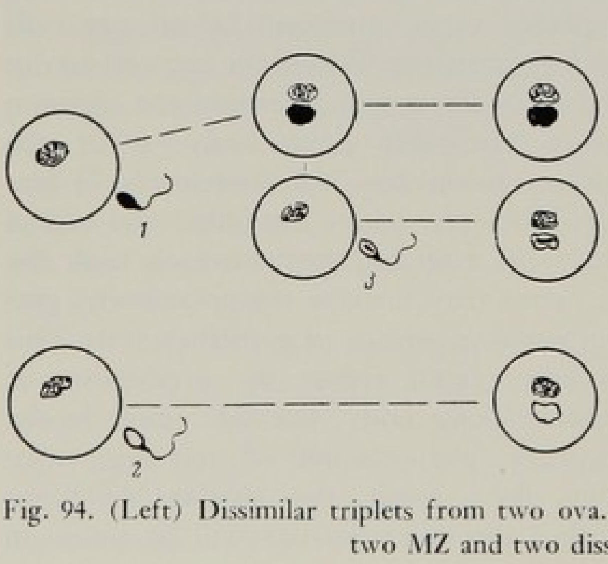
Fig. 93. Uniovular triplets with one dissimilar member and two similar MZ twins.

the same pregnancy (Fig. 93).

The production of two genetically dissimilar twins, or triplets with one dissimilar and two similar members, may be further complicated by the fact that the possibility of pluriovulation, even though insufficient by itself, cannot be discounted (Curtius). Should a second egg, separately implanted, become fertilized simultaneously with the conception of uniovular oocytic twins, the result would be three genetically dissimilar twins from two eggs (Fig. 94). Fertilization of another egg in conjunction with the conception of uniovular triplets (two similar and one dissimilar, as in Fig. 93) would give rise to quadruplets, two similar and two dissimilar both to the first pair and to each other (Fig. 95.)

Similarly, Curtius' theory regarding genetically alike twins may be summarized as follows: In the case of identical twins, if fertilization takes place at a more advanced stage than the second maturational division, at a time when this division can no longer be influenced, it cannot result in the emission of a second fertile polar body. The alternative would be that when fertilization occurs after emission (alteration in the genetically controlled rhythm), the elimination of the second polar body either is beyond the stage of interference or already has been effected. Consequently, the G factor would be able to act only on the mature and fertilized egg cell, inducing it to split into two completely equivalent daughter cells, each of which would possess the same nuclear and protoplasmic structure. Genetically speaking, this method of producing two equivalent twins would be similar to what happens in the zygotes of invertebrates according to the total equivalence principle of the first two blastomeres (Driesch, 1891 and Herbst, 1900).

However, the situation is different in mammals, where the first two blastomeres are not equivalent either morphologically or embryogenetically. In the opinion of Curtius and Sobotta, one blastomere is cho-



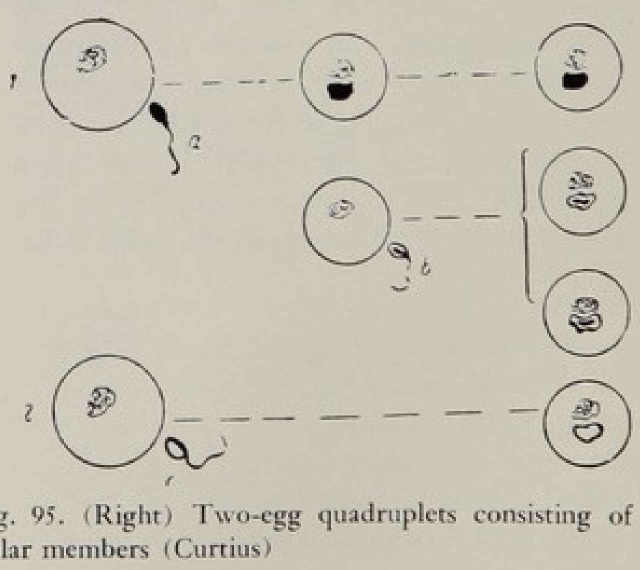


Fig. 94. (Left) Dissimilar triplets from two ova. Fig. 95. (Right) Two-egg quadruplets consisting of two MZ and two dissimilar members (Curtius)

sen to form the fetus, while the other gives rise to the extra-embryonic membranes (chorion and ectoplacenta). At first the G factor remains latent, forming two embryonic structures only in the period of the embryonic area. In addition, by acting on the second blastomere, it duplicates the trophoblast and thereby produces the two chorions generally observed in dissimilar twins. The question of which of the two mechanisms of gemellogenesis—in the period of two blastomeres or in that of the embryonic area—is usually at work was left open by Curtius (1932). However, he agreed with Hertwig and with v. Verschuer that both mechanisms are possible.

Several years earlier (1926), Dahlberg's theory of one-egg and two-egg twinning was formulated. His explanation was based on the premise that there is a kind of race going on between the processes of maturational meiosis and twinning. In a diagram (Fig. 96) he showed that even quadruplets may arise by a continuous series of minor divisions, according to Hellin's Law. This process occurs in every $\frac{1}{n} \times \frac{1}{n} \times \frac{1}{n} = \frac{1}{n^3}$ cases, where $n = 80\text{-}90$, while the quadruplets produced would be those numbered 4, 5, 6 and 7. With the reduction division taking place at different stages of this series of gemellogenetic divisions, it is clear that the earlier it occurs, the more it would tend to establish genetic equivalence in the following gemellogenetic divisions. On the other hand, the later it occurs the more it would be likely to produce genetically different twins. According to Dahlberg, various combinations may be explained in this way, including those of monozygotic, dizygotic or trizygotic triplets.

The same principle of a presumed competition between meiosis and twinning was applied to explain a combination of similar and grossly dissimilar twins. A very early gemellogenetic division would give rise to

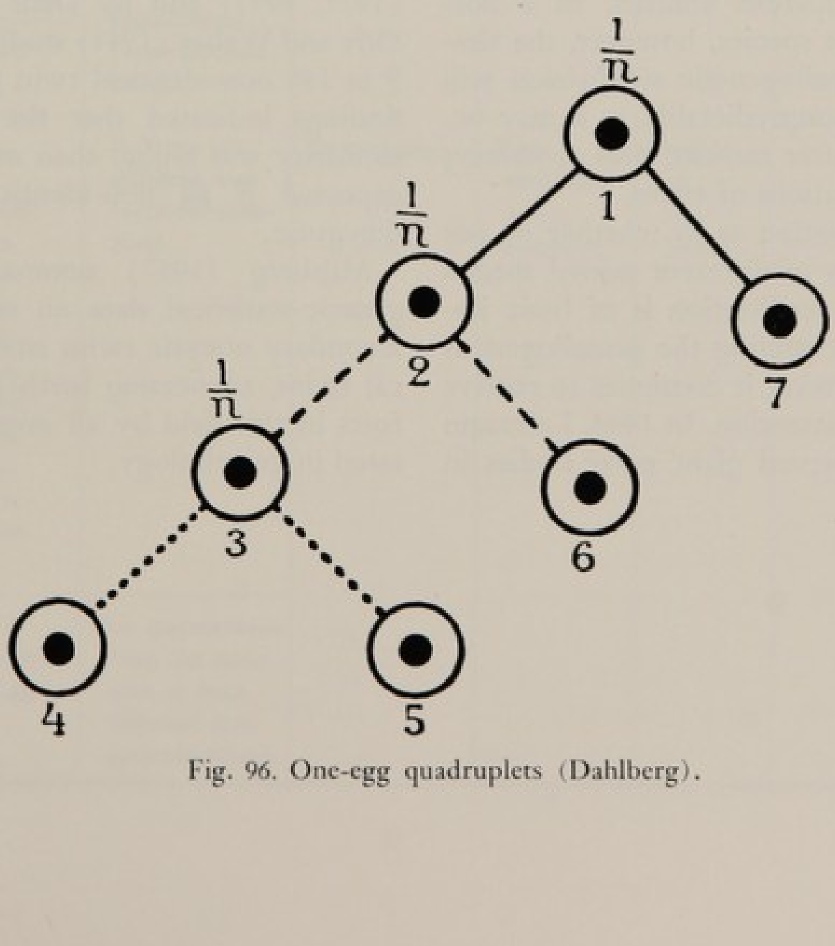


Fig. 96. One-egg quadruplets (Dahlberg).

Graafian follicles with two egg cells instead of one (Rosner, 1901 and Quenot, 1903), or even to two egg cells in two follicles situated closely together in the same ovary and released simultaneously. Prevalence of the latter phenomenon may be genetically determined in most plurizygotic multiparous animals.

Regarding dizygotic twinning in man, Dahlberg supported Strassmann's contention that the placentae of such twins often tend to be joined together in some way. Therefore, the respective ova will be derived from the same follicle and remain together, being held on top of each other by the granulous cells surrounding the ova when they reach the uterus.

In the armadillo, however, where this gemellogenetic subdivision consistently follows the process of meiosis, the same process is known to lead to the formation of monozygotic twins. With the pluriovular organization of gemellogenesis not completely established, monozygotic twins may also be found in multiparous animals. In a normally uniparous species, however, the timing of the gemellogenetic subdivision will be particularly unpredictable, as it may occur before or after meiosis, thus producing various combinations of twins.

Since the question as to whether or not the polar bodies of different animal species are capable of fertilization is of basic importance in interpreting the gemellogenesis of human DZ twins, it continues to receive a good deal of attention. In 1944, Lehmann and Huber observed giant polar bodies in the *Tubifex* and in this connection discussed the possible existence of twins intermediate in their genetic structure between MZ and entirely dissimilar DZ twins. Calling this type "ovozytäre eineiige Zwillinge" (PZ), i.e. uniovular *oocytic* twins, they suggested that these twins possess identical chromosomal heredity on the mother's side and a different one on the paternal side. This notion was supported by Rosin (1947) who stressed that if some DZ pairs show greater resemblance than ordinary sibs, they might conceivably be oocytic twins. He followed through by devising a special method for estimating the frequency of this type of twin pair under various conditions.

A schematic review of all possible mechanisms which may result in twinning is presented in Table XXX.

Blood group studies have been used to test the theory of the existence of oocytic twins. Following researches on the distribution of the ABO and MN blood groups in non-identical twins by Schiff and v. Verschuer (1931, 1933) and by Dahr (1941), Dahr, Offe and Weber (1941) studied blood group P in 188 non-identical twin pairs, and their findings indicated that the frequency of similarity was higher than might have been expected if all non-identical pairs were dizygotic.

Mijsberg (1957) summarized previous genetic-statistical data on the presence of secondary oocytic twins among non-identical twins, advocating further combined efforts in this field by all investigators interested in gemellology.

Table XXX
POSSIBLE VARIATIONS OF TWINNING

<table>
<tr><th colspan="2">Through Female Gamete</th><th>Through Male Gamete</th><th>Onset of Twinning</th><th>Fetal Membranes</th><th>Placenta</th><th>Ovularity</th><th>Zygosity</th></tr>
<tr><td rowspan="4">Single egg cell</td><td>With G factor</td><td rowspan="2">One spermatozoon with or without G factor</td><td rowspan="2">In the period of 1. Embryonic disk or primitive line, 2. blastocyst, 3. two blastomeres</td><td>One chorion and amnion</td><td rowspan="2">Single</td><td rowspan="4">uniovular</td><td rowspan="2">MZ</td></tr>
<tr><td>Without G factor</td><td>One chorion, two amnions</td></tr>
<tr><td>With G factor present or received through spermatozoon fertilizing the second polar body</td><td rowspan="3">Two spermatozoa: 1. From the same man in one intercourse, 2. from the same man in different intercourses (superfecundation), 3. From two different men (superfecundation)</td><td rowspan="4">In syngamy</td><td rowspan="4">Two chorions and amnions</td><td rowspan="4">Double or con-joined</td><td rowspan="4">DZ</td></tr>
<tr><td>with two nuclei</td></tr>
<tr><td rowspan="2">Pluri-ovulation</td><td>In the same ovulation: 1. 2 ova from 2 follicles derived (a) from 2 ovaries, (b) from 1 ovary; 2. 2 ova from one follicle</td><td rowspan="2">biovular</td></tr>
<tr><td>In two successive ovulations</td><td>Two spermatozoa from the same man or from different men (superfetation).</td></tr>
</table>

Chapter VIII

TWIN PREGNANCY: ITS PHYSIOLOGY AND PATHOLOGY

CHARACTER AND POSITION OF MEMBRANES IN TWIN PREGNANCY

THE POSITION of the membranes of ovular origin (chorion, amnion), maternal origin (decidua), and mixed origin (placenta), is of considerable importance in establishing a connection between mother and fetuses and between the fetuses in multiple pregnancy.

Before discussing this point, however, it would be helpful to consider whether the genetic and obstetrical classifications of twin births coincide. The question is, do twins who bear a strong resemblance to each other, and are apt to be diagnosed as monozygotic according to genetic criteria, correspond to the monochorionic twins of obstetrical classification, and do twins who do not resemble each other, that is dizygotic pairs, correspond to dichorial twins? Such, in fact, was the common belief until the 1920's. Even today there is a tendency on the part of some investigators to regard twins born with a single chorion as monozygotic. Nevertheless, as will be seen, this criterion has value only as an approximation, for the assumed equivalence does not exist in a number of cases.

Siemens (1925) was the first to raise the question by describing one monochorionic DZ pair and six dichorial MZ pairs. The latter series included Waardenburg's twin daughters who at birth showed a single placenta, a double amnion and a double chorion. This particular case is considered a classic not only for its scientific conclusiveness, but because the father, being a geminologist, was later able to confirm the diagnosis of monozygosity on the basis of the physical and mental characteristics of his two daughters. Waardenburg himself wrote two reports on them (1926-1929), and we are indebted to him for permission to reproduce their original photographs, which confirm the identicalness of these distinctly dichorial twins (Fig. 97-99).

Commenting on photographs of his twins at age six, Waardenburg wrote, "One can see quite clearly the same build and habitus, the same color and texture of hair and the same slight degree of 'scapulae alatae.' Later on these twins clearly showed that they were completely MZ both physically and psychologically. They had the same talent for drawing and singing, were both musical, and behaved in exactly the same manner at school. I could not even distinguish their voices unless I saw them. Today they are 25 years old and even now people cannot distinguish between them. . . ."

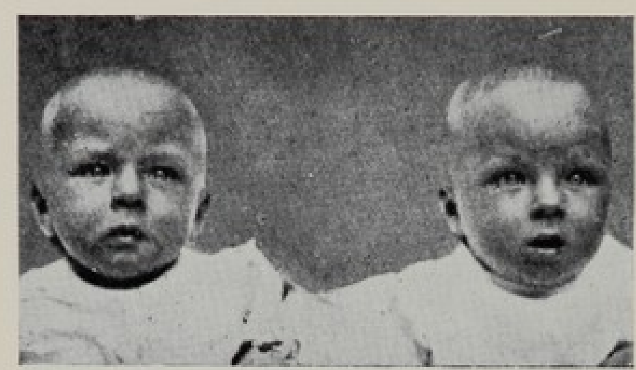
Studying 24 twin placentae with the stereoradiographical method, Kiffner (1929) showed that the common practice of classifying MZ twins as monochorionic and DZ twins as dichorial could not be considered reliable. In reexamining the cases studied by Kiffner and adding other new ones, Curtius (1930) used the similarity method in diagnosing the given twins. In a series of 24 DZ pairs, Curtius noted dichoriality in 23 cases. He assumed monochoriality in one same-sex

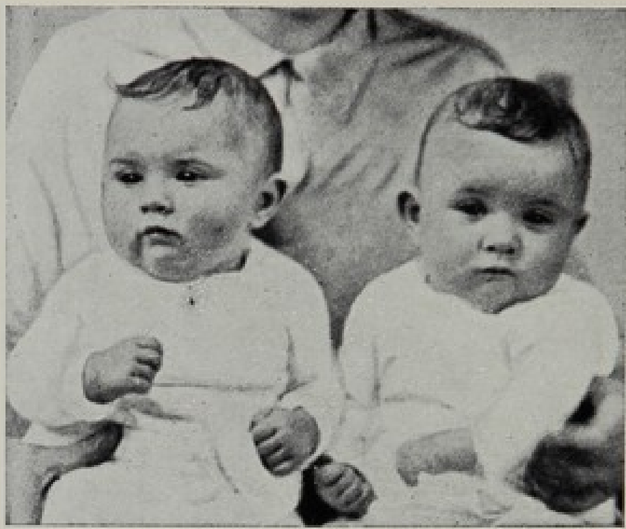
Figs. 97-99. Waardenburg's dichorial MZ twins at the ages of six years (upper left and right) and 11 years.

pair, since he was able to isolate macroscopically two laminae (supposedly amniotic) in the dividing septum.

In six MZ pairs, Curtius was surprised to find three monochorionic and three decidedly dichorial pairs. Among the latter, two pairs had a double placenta. The photographs of the three dichorial MZ pairs are shown in Figures 100, 101 and 102. Curtius concluded that hereditary identicalness and monochoriality are not at all the same thing; the presence of a single or double chorion in twins does not depend only on their derivation from one or two eggs. The position of the chorion seems to be more decisively determined by the distance separating the two implanted ova, as has been shown by Lenz.

In our opinion, the question as to the greater or lesser distance between implanted ova arises only in regard to the membranes of biovular twins. For uniovular ones, we should perhaps think of the relative distance between the embryogenic structures after the splitting of the single fertilized ovum.





Figs. 100-102. Three pairs of dichorial MZ twins (Curtius).

In 1931 Lassen reviewed the cases studied by Curtius and increased the series to a total of 56 pairs in whom the membranes had been studied macroscopically and microscopically, and the similarity method applied. The nine monochorionic pairs were confirmed by the similarity method as being of equal heredity. Of the 47 dichorial pairs, 21 were of opposite sex, 21 of the same sex, though of different heredity, and five of the same sex and equal heredity.

Thus Lassen found five dichorial twins in a series of 14 MZ pairs, showing that the occurrence of dichorial MZ twins is not a rarity. She also used the similarity method for a comparison of monochorionic and dichorial MZ twins, but failed to detect any difference between them. The intra-pair similarity was the same in the two groups for all the characteristic features examined. It may therefore be said that both groups include genuine MZ twins, that is, twins of equal genotypes. The observed ratio of approximately 1:2 for dichorial and monochorionic MZ twins, as found by Lassen, is certainly very high, but this may have been due to the limited number of cases.

The findings of Curtius and Lassen were confirmed by Steiner (1935) in a series of 132 twin pairs classified according to mem-

Plate I. Bichorionic MZ twin sisters 13 years of age (observed by Gedda).

Plate II. Monochorionic DZ twin brothers 8 years of age (observed by Gedda).

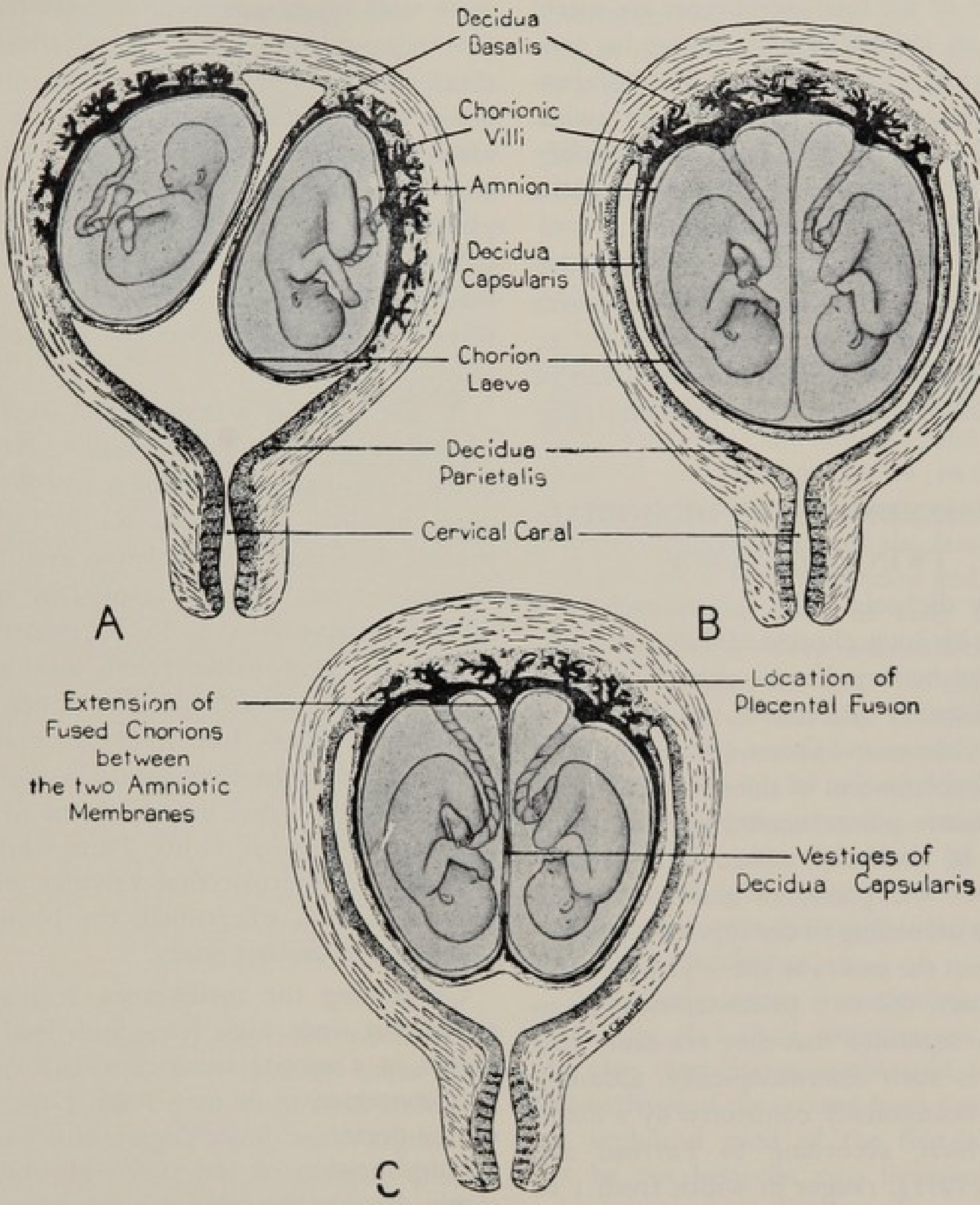


Fig. 103. Fetal membranes in twin pregnancies (Patten): (A) total separation of the membranes in biovular twins; (B) uniovular twins; (C) fusion of the membranes in biovular twins.

branes and to the similarity method. While 32 pairs were both monochorionic and monozygotic, 76 of the remaining 100 dichorial pairs were dizygotic, and 24 monozygotic. Among the latter (dichorial monozygotic), 16 pairs had a double placenta, leading Steiner to regard dichoriality in MZ twins as being fairly common. He also concluded that the division resulting in MZ twins occurs before implantation of the egg in the mucous membrane of the uterus and before the embryonic differentiation from which the chorion is derived.

It may be seen, therefore, that the characteristics of the fetal membranes are useful only as an indication and cannot be considered as a reliable criterion for differentiating monozygotic and dizygotic twins. It would certainly be a mistake to classify all monochorionic twins as monozygotic, and all dichorial twins as dizygotic.

At this point it is pertinent to examine the different conditions arising in the uterus when the products of conception show the various possible combinations which can be found obstetrically in the membranes (Fig. 103).

FETAL MEMBRANES IN DICHORIAL TWIN PREGNANCY

Clearly dichorial pairs, where each twin possesses his own chorion, amnion and placenta, may be found to be either closely or rather distantly imbedded in the uterine mucosa. Gernez and Omez (1938) observed that the implantation of the ova at two relatively distant points occurs only in seven percent of dichorial twins. The characteristics of the placentae and membranes may vary according to the type of implantation. When the embryos are implanted rather far apart, the two placentae may be so distinctly separated that they are easily recognized as such macroscopically, although they are occasionally connected by a membrane which, according to Favreau and Beurois (1933), ranges in width from 1 to 13 cm. On the other hand, when the two surfaces of implantation are close to each other, they may be more or less coherent, thus giving the impression of a single placenta.

In line with the investigations of Hyrtl (1870) and Schatz (1884), it may happen that the two extrafetal circulatory portions of each placenta, although developed together and appearing to be one, remain separate with no communication between the two independent systems. The studies were conducted by injecting substances into the blood stream, making it possible to trace vascular branching. This method was subsequently improved (radiography of the placenta following injection of radiopaque substances). It has been proved, however, that the two placental circulations are not always completely independent in dichorial twin pregnancies.

A case in point was described by Porak in 1897, with a blood vessel linking the two umbilical cords, and a similar one by Béquain in 1910. Later on, Kadjar (1927) studied the placental circulation in all cases available at the Tarnier Hospital by means of stereoscopic x-rays. In four instances there were anastomotic vessels uniting the two placentae of dichorial twin pregnancies. Using x-rays, Lassen (1931) also observed vascular anastomoses in a dichorial twin pregnancy, but it turned out to be a case of dichorial MZ twins. Thus, while the existence of interplacental vascular anastomoses has been ascertained, the phenomenon calls for further study.

Concerning the membranes, it may be noted that since each fetus finds itself enclosed in a special amniochorionic cavity, it is contained in its own fluid. Depending on the greater or lesser degree of proximity of implantation of the two embryos, one single decidua may envelop the two chorionic sacs, thereby forming a single cavity for incubation. Or it may double itself and form two separate involucra—one for each embryo. In the first instance, the two embryos are separated by four distinct layers represented by two chorionic and two amniotic laminae. In the second instance, the embryos are separated by six layers, including both layers of the two separate deciduae.

FETAL MEMBRANES IN MONOCHORIONIC TWIN PREGNANCY

Monochorionic twins share the same placenta. Though each twin possesses its own arteriovenous circulation, there may be a so-called *third circulation* in the placenta, consisting of a system of both superficial and deep blood vessels running between the fetoplacental circulations of the two twins. Obviously, the conditions of intrauterine interfetal circulation are of utmost importance in the pre- and postnatal physiology and pathology of monochorionic twins.

Resinelli and Ferroni (1940) observed that, in perfectly normal conditions, these anastomoses are arranged in such a way that neither fetus possesses any advantage over its twin. Not infrequently, however, the third capillary circulation, passing from the first to the second fetus, is not equal to that passing from the second to the first. When the superficial anastomoses cannot compensate for the disparity of the deep vessels, a circulatory asymmetry is established, which later becomes the cause of functional and anatomical alterations in the bodies of the fetuses.

In such cases, it has been assumed by Viana that a fight for survival takes place in the maternal uterus, sometimes ending in the death of one of the twins. Various differences of prenatal development, observable in some pairs of uniovular twins, may be produced by such an asymmetry of the third circulation, and result in a number of pathological conditions.

As to variation in prenatal development, Zangemeister claimed that differences in weight and length are seen in 95 percent of uniovular twins. The greatest differences noted by him were 3200 gm. in weight and 13 cm. in length. In 172 twin births, Sövényhàzy noted a difference between monochorionic twins of 1250 gm. in one pair, and in three cases one of 1000 gm. In fact, in a pair of monochorionic and biamniotic twins, Craciotto (1938) observed a weight difference at birth of 1600 gm. (resp. 3900 and 2300 gm.) and a difference of 5 cm. in length, with absence of the nucleus of ossification of the cuboid bone only in the second-born.

The existence of interfetal circulatory anastomoses had been known to earlier authors, but was most clearly demonstrated by Hyrtl (1870) and Schatz (1884). On the basis of his findings in 24 twin births, Schatz noted three circulatory systems: the first and second represent the fetoplacental circulations of both organisms and are connected with the heart of each twin; the third consists of deep anastomotic vessels running between the first two circulations, and is known as "the area of transfusion." These anastomoses are formed in such a way that arterioles of one circulation unite with venules of the other circulation, bringing blood from the left heart of the first fetus to the right heart of the second. It was this hydraulic system that Schatz called the third circulation.

Apparently, earlier investigators had realized only that these anastomoses between the two circulations could lead to a fatal hemorrhage of the second-born twin, should the umbilical cord of the first-born twin not be cut between two ligatures. Schatz was the one who discovered an active hydraulic factor in this third circulation during the intrauterine existence of the two fetuses as the possible cause of harmful effects.

With a marked degree of asymmetry in the third circulation, great differences may arise in the prenatal development of monochorionic twins, as well as certain pathological conditions. According to Schatz, the connection established between the twins by means of the third circulation may result in the stronger fetus (donor) transfusing venous blood into the placental villi which send arterialized blood into the circulation of the weaker fetus (receptor). Gradually, the receptor shows signs of general failure, such as hypertrophy of the heart, relative polyuria, hepatosplenomegaly, and ascites, and there is polyhydramnios. While this fetus may die or become acardiac, the donor may also sustain damage by pumping most of his venous blood into the circulatory system of his twin.

In 1922 and later in 1928, Mutel and Vermelin proposed a new theory concerning the circulatory connections between two monochorionic fetuses. Fetal transfusion from the donor to the receptor may take place either actively through arterial anastomoses, blood being pumped from the heart of the donor, or through venous anastomoses which passively receive blood from the donor. In the former instance, the donor may show hypertrophy of the heart, liver and spleen, overdevelopment due to increase in nutritional exchange, ascites, polyhydramnios. In the latter case, the donor will show anasarca, ascites, oligoamnios. The donor would be the fetus possessing a greater number of arterial vessels, while the receptor would be the one with a larger venous system.

Injecting colored substances (cinnabar

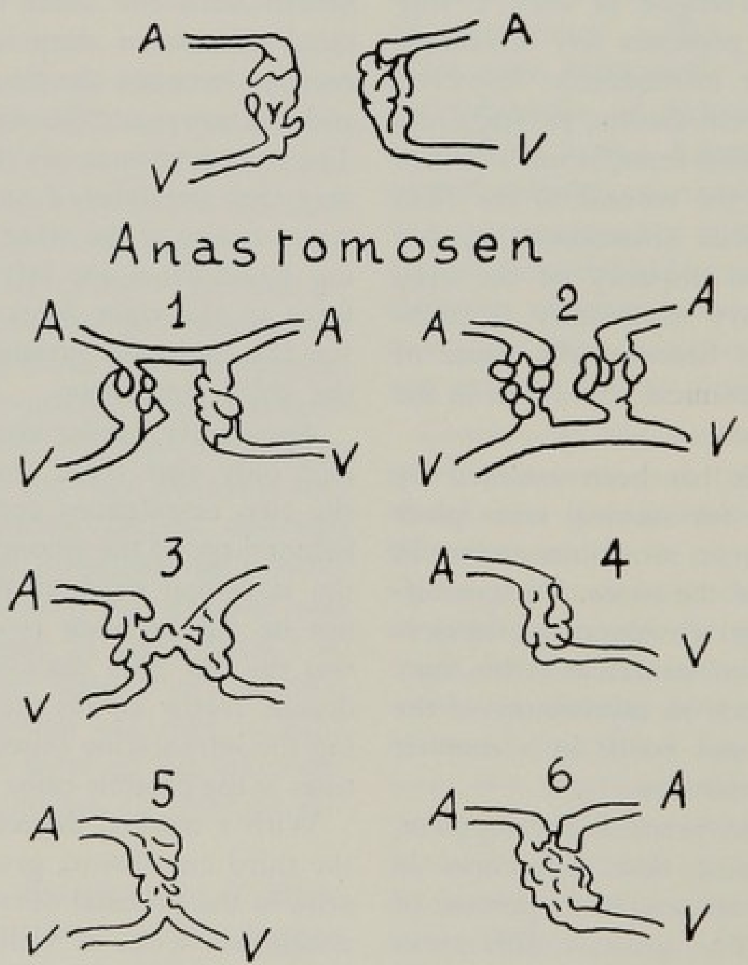


Fig. 104. Placental circulation in monochorionic twins with various types of anastomoses (Wenner) (Anastomosen=Anastomoses.)

suspended in gelatine) or radiopaque substances (barium sulphate) into the vascular system of five monochorionic placentae, the same investigators found an absence of the third circulation in two instances. When it does exist, this system may be of three types: deep anastomoses, superficial anastomoses, or a combination of superficial and deep anastomoses. The function of the superficial anastomoses would be to maintain an equal pressure in the two fetoplacental circulations and contribute actively to the equal growth of the two organisms. The action of deep anastomoses may disturb the two circulations when cardiac overfunction in one fetus unilaterally increases the arterial flow or the venous aspiration in the other. Such imbalance could be compensated for in one of two ways: either by a tendency of superficial anastomoses to neutralize the unequal pressure in the two fetoplacental circulations; or by the development of a second deep anastomotic branch which would be equal in volume to the first but hemodynamically opposed to it.

More recently, Wenner (1947) studied placental circulation in monochorionic twins by injecting the vessels with an acetone solution of celloidin. Following its solidification, the tissues are corroded by acids, leaving a cast of the circulatory system. The observed anastomoses, apart from being superficial or deep, were shown to vary in type (Fig. 104).

In a study of the vessel pattern of five monochorionic and one dichorial placentae, De Camillis and Tammeo (1948) made the venous circulation visible with a suspension in water of barium sulphate and, sometimes, *ioduron*, and the arterial circulation with a solution of cinnabrin. In this way they were able to examine the systems by direct observation as well as by photographs and x-rays, and succeeded in establishing the number, volume, position (superficial or deep) and nature of such anastomoses.

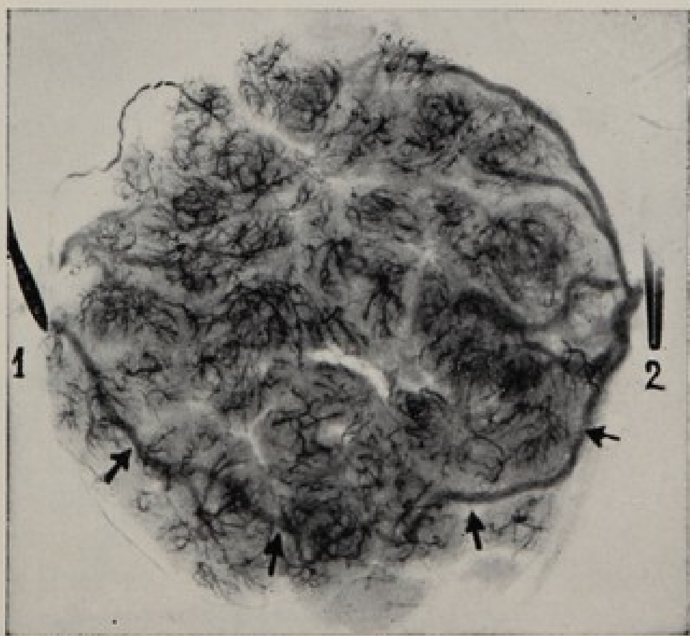


Fig. 105. Circulatory symmetry and hemodynamic balance (due to superficial veno-venous anastomoses as indicated by arrows) in monochorionic placenta injected with 30% *ioduron* solution (De Camillis and Tammeo).

These investigators showed, for instance, that superficial anastomoses may be arterio-arterial or veno-venous, while deep anastomoses are always between artery and vein. Superficial veno-venous anastomoses (containing arterial blood) would cause no hemodynamic disequilibrium between the two placentae. On the contrary, they would help to maintain such equilibrium by functioning as a valve, while the

Fig. 106. Vascular network in monochorionic placenta injected with a barium sulphate solution (De Camillis and Tammeo).

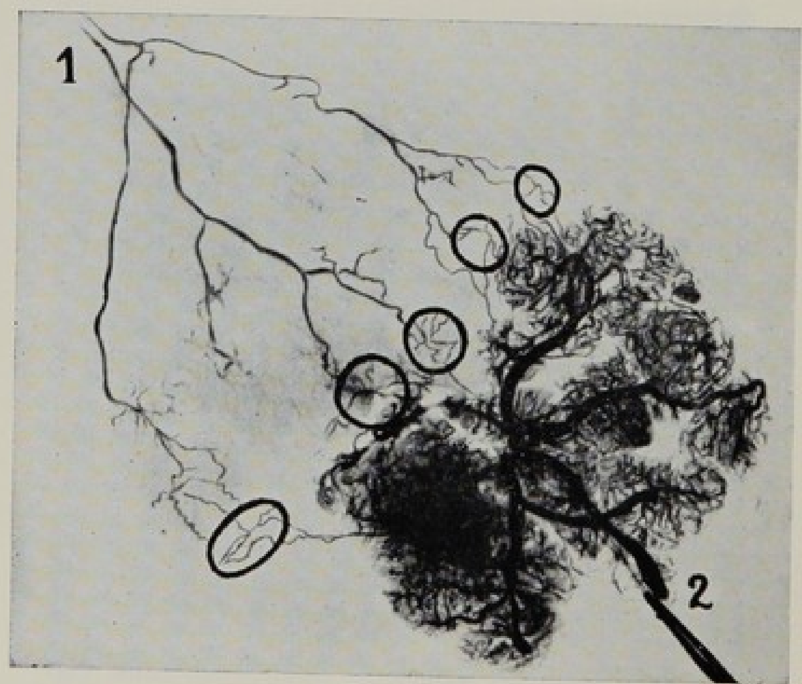


Fig. 107. Deep arterio-venous anastomoses (third circulation) in monochorionic placenta injected with a cinnabrin solution (De Camillis and Tammeo).

arterio-arterial anastomoses (containing venous blood) would produce a disequilibrium. More important are the deep anastomoses which produce a double flow.

Ordinarily (that is, under conditions of equilibrium) the arterio-venous anastomoses functioning in one direction correspond to the number of such vessels functioning in the opposite direction. When the equilibrium is upset, however, the asymmetry may reflect on the fetuses to such an extent that differences up to 950 gm. in weight occur, as described by some authors. Several illustrations provided by De Camillis and Tammeo will help to explain the important problem of vascular anastomoses in the placenta of monochorionic twins (Figs. 105-108).

double amnion. In a small percentage of cases, however, they may be monoamniotic. Viardel (1671) was the first to note that in certain twin pregnancies the amniotic cavity may be single, an observation confirmed by Smellie (1754).

As to the frequency of monoamnion in monochorionic pregnancies, opinions differ widely. In Holland, monoamnion was found by Voûte in 4% of uniovular twins, 66% being monochorionic and biamniotic, and 30% dichorial and biamniotic.

A rather frequent occurrence in monoamnion (up to 54% of the cases, according to some authors) is a coiling or knotting of the umbilical cords, which may result in the death of one or both twins. As mentioned previously, it happens only very rarely that

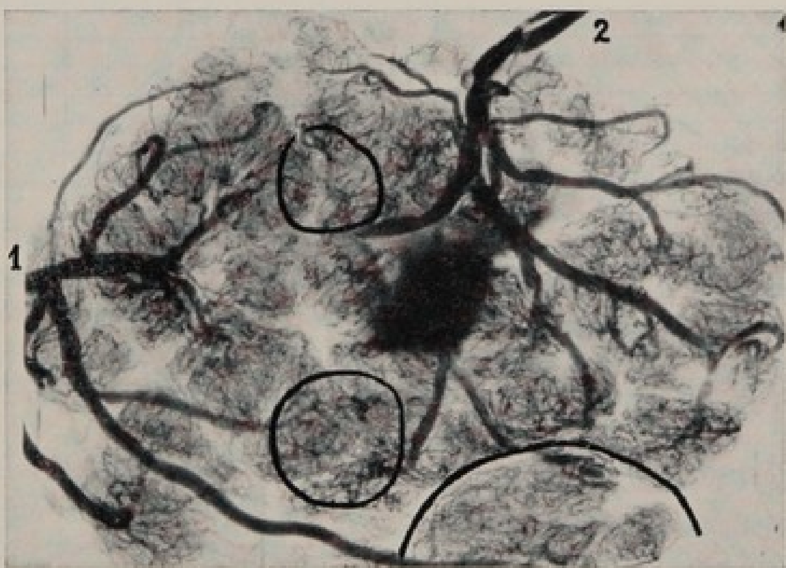


Fig. 108. Circulatory asymmetry and hemodynamic disequilbrium in the placenta of monochorionic twins born prematurely (stillborn) with a weight difference of 500 gm. (De Camillis and Tammeo).

The confluence of the two fetal circulations with the third may lead to the development of a macrocardius in one fetus and a microcardius in the other. Or it may result in an acardiac twin.

As a rule, monochorionic twins possess a

monochorionic twins are also monoamniotic. Whether such a monoamnion is interpreted as primary or secondary (it may also occur in dichorial twins, but always exceptionally), it necessarily causes the twins to share the same amniotic fluid. Sometimes it is accompanied by an umbilical cord which is single for the greater part of its length, only dividing in two at the level of the umbilicus. This observation explains why unifunicular monochorionic twins or *omphalopagi* are always monoamniotic. Such twins easily cause reciprocal damage, especially during confinement when complications, such as the coiling of the umbilical cords, are frequent.

The septum between the two sacs of uniovular twins may be formed by two amnia which adhere to each other. In biovular twins the septum consists of two amnia and two choria which are fused together with atrophic villi.

DURATION OF TWIN PREGNANCY

It is commonly believed, and probably true, that in the majority of cases the duration of a twin pregnancy is shorter than that of a single pregnancy. According to Mauriceau, it is an undeniable fact that a woman with a twin pregnancy does not bear it as long as she would a single one. However, this statement cannot easily be documented, since the criterion of the stage of development reached by the fetus at birth (which, together with the date of the last menstruation, allows a calculation of the duration of single pregnancies) is absent here.

Pinard and Bachimont estimated that the average duration of twin pregnancies is 269 days if the mother rested during the later months (average weight of the two fetuses 2850 gm. and 2480 gm.), and 247 days if she worked up to the time of her confinement (average weight of the two fetuses 1935 gm. and 1900 gm). Available statistics include those of Vaccari, who computed the duration in 154 cases of twin pregnancy. On the basis of the data shown in Figure 109, he concluded that most twin pregnancies terminate at between 7 and 8½ months.

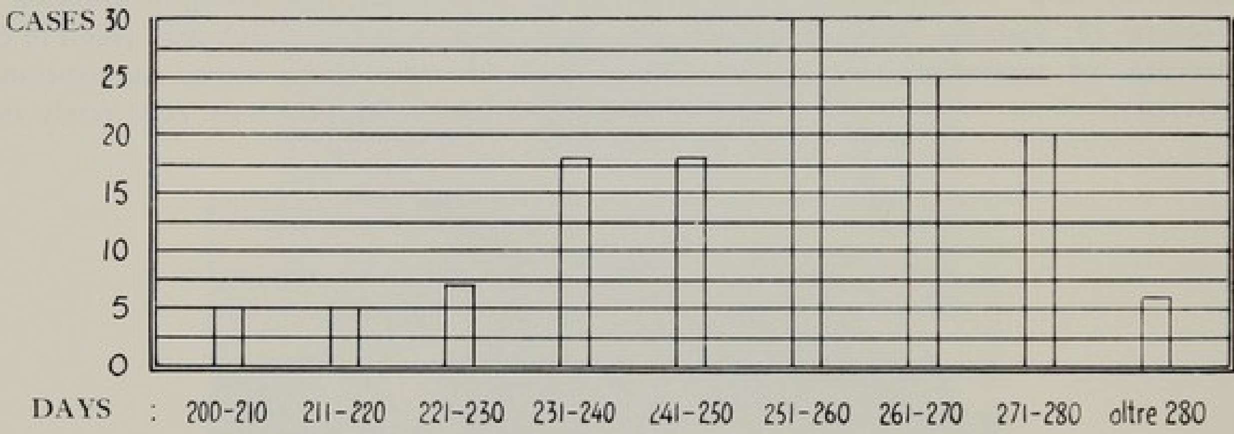


Fig. 109. Variations in the duration of twin pregnancies (Vaccari). (Oltre=Over.)

This figure agrees with those obtained by Gernez and Omez from 226 twin pairs observed at the Clinique d'Obstetrique de la Charité de Lille. The following percentages were obtained: 14.15% pregnancies delivered normally at term; 35.46% at 8½ months; 17.70% at 8 months; 10.61% at 7½ months; 5.75% at 7 months; 6.63% at 6 months.

The cause of premature births may lie in what Hoehne calls "the greater mechanical and chemical load" that the mother of twins has to support. The greater mechanical burden is due chiefly to excessive distension of the uterus which causes expulsive contractions, while the greater chemical load may depend on varying degrees of toxemia of pregnancy. Primiparae are more frequently affected by these conditions than are multiparae.

The actual duration of twin pregnancies can be deduced from the characteristics of each fetus, as in single pregnancies. The diagnosis, however, is more difficult because it is often unclear whether the frequent fetal underdevelopment should be ascribed to prematurity or interpreted as caused by the greater difficulties of the twin pregnancy.

Leudin (1934) and I. Yang (1935) studied this question and obtained the following results:

1. The length of mature twins is not essentially different from that of infants born singly.
2. The weight is more variable and usually reduced in comparison with that of single born infants (on the average 200-300 gm. less).
3. For twins, too, length rather than weight is the most reliable basis for determining the duration of pregnancy.
4. The analysis must be based on the most developed twin, i.e., the taller and heavier child.
5. Labbart's method may also be used for twins. From a large material, analyzed by means of a binomial formula, Labbart constructed a table showing the duration of pregnancy for each separate length of the fetus.

In line with the findings of Ylppö (1919) and Lunde (1930), the mortality of premature twins is a little lower than that of single born children of the same weight.

DIAGNOSIS OF TWIN PREGNANCY

Another obstetrical problem of particular interest is that of diagnosing the presence of twins. From a clinical standpoint this diagnosis is important not only for the purpose of establishing a multiple pregnancy as such, but for other aspects that make for successful delivery, such as determining the position of the fetuses in the uterus.

One fact is generally noted when case histories are obtained—mothers very seldom know they are bearing twins. Sometimes, especially if twin births run in the family, the mothers have some inkling of it because of either the exceptional size of their abdomen, or excessive disturbances in their sympathetic nervous system, or unusual symptoms caused by compression and fetal movements. However, family history and observed signs are rarely sufficient to arouse the mother's suspicions, so that she usually reaches her confinement in the belief that she is carrying only one child.

Although many mothers are under the care of a family physician, even conspicuous signs of a twin pregnancy are often overlooked. Even in so outstanding an example as the Dionne quintuplets, Dr. Allan R. Dafoe, who attended the mother during her pregnancy, stated afterwards that he was not able to make any diagnosis of multiple pregnancy because, on examination, the uterine tissues were abnormally swollen, being impregnated with serum. The obstetric auscultation was not conclusive.

Besides taking into account the presence of twins in the family history in diagnosing a twin pregnancy, the doctor might look for the following signs which are briefly described in the order of their appearance:

During the first half of the pregnancy: Exaggerated dysfunction of the sympathetic nervous system (abundant salivation, heartburn, frequent vomiting); marked gestosis due to the increase of hormones in the circulation; overproduction of chloasma; size of pregnant uterus disproportionate according to time of last menstruation. Brindeau points out that an important clinical sign, at least for monochorionic twin pregnancies, is that of an early acute polyhydramnios. During the first months, however, the diagnosis is always difficult.

During the second half of the pregnancy: Considerable increase in abdominal circumference, which reaches a length of over one meter much before term, and gives rise to the formation of many new striae. The uterus attains a length of 40 cm. or more towards the end of the pregnancy. Lying and walking become difficult due to a noticeable slackening of tissues or an aching of the pelvic articulations and also an accentuated lordosis. Signs of sympathetic nervous system dysfunction may extend into the second half of the pregnancy (Manzi, 1909), together with various circulatory, respiratory, intestinal and renal disturbances (see complications of twin pregnancy).

On palpation a strong tension is noted, giving an impression ranging from that of a contracted uterus to a uterus pausing between two contractions in a simple pregnancy (Favreau and Beurois), or similar to a rubber bag filled with air or water (Pinard). The uterus is in high tension and is liable to contract on palpation. Nevertheless, in the eighth and ninth months many fetal parts may be felt, especially the two heads and two buttock regions. Sometimes on both sides, sometimes above and below, small parts correspond to various points on the abdomen where the mother feels vigorous movements.

From the seventh month on, auscultation shows that the fetal heart may be heard at two distinct points separated by a silent zone, especially when two doctors auscultate the two points at the same time and note that a different rhythm of pulsation exists between them. The double heartbeat may give rise to Arnoux's sign, which consists of an alternating rhythm of synchronism and asynchronism. Kautsky (1921) compared it to the sound made by a pair of trotting horses.

Boero (1916) held that even a single focus of auscultation, provided it is intense and accompanied by a voluminous uterus under tension, indicates the possibility of a twin pregnancy. The same is true for a rough and intense murmur at different points as observed by Hohl. Smith (1941) originated some stethograms and recordings of the fetal heartbeat in twin pregnancy.

On exploration, the movements induced on the presenting part are not transmitted to the opposite part. Moreover, a passive dilatation of the cervix is noted before contractions occur (these being explained by mechanical reasons) until there is an opening of the uterine orifice up to 2 - 3 cm. The head may also become fixed before the rupture of the membranes.

Another diagnostic criterion mentioned by Heilmann (1930) is the occurrence of intrauterine singultus from the fifth month. Parenthetically, it may be noted that Gerin-Lajoie (1939) observed a negative Ascheim-Zondek in a case of twin pregnancy with one ovum in the uterus and the other in one of the Fallopian tubes.

In modern medicine, radiology is generally decisive when a twin pregnancy is suspected (Albano). The x-ray technique is now widely used for detecting crania and spines. By this means one diagnoses not only a twin pregnancy but the type of presentation as well.

FETAL POSITION AND PRESENTATION

Obviously, the diagnosis of twin pregnancy must be augmented by that of the position the twin fetuses assume in the womb. The term "bilateral position" is used when the sagittal plane of the uterus passes between the twins. The abdomen then shows a dilatation which is chiefly lateral. The fundus of the uterus is often forked, or it may be heart-shaped (Hergott), or divided into two halves by a longitudinal ridge.

The term "anteroposterior position" is used when the frontal plane of the uterus passes between the twins. In that case marked signs of suprapubic edema may be observed, while the abdomen protrudes almost as a point (Resinelli-Ferroni). The anteroposterior position, which according to Pinard does not exist, is a rare condition. That it occurs has been shown by the cases of Guillement (1898, 1924) and Anderodias (1924).

A "vertical position" is observed when the twins are in a transverse position, one above the other. The fetuses may also assume the position of an upright or an inverted T (T or ⊥). According to Favreau and Beurois, this position, with one fetus in a vertical and the other in a transverse presentation, is almost as frequent as that of juxtaposition.

As to the data of presentation, the reports follow two patterns, one describing each twin separately (see Table XXXI), and the other considering the two twins together (see Table XXXII). The main conclusions to be drawn from these data are as follows:

Table XXXI

TYPES OF PRESENTATION OBSERVED IN THE DELIVERY OF TWIN SUBJECTS (%)

Type of Presentation	*Investigators*			
	Krahn	*Sriber*	*v. Marc*	*Vaccari*
Vertex	64.28	61.3	63.3	67.54
Forehead	—	—	—	1.31
Face	—	0.84	—	0.33
Breech	28.86	30.8	31.1	25.90
Shoulder	6.25	5.7	5	4.92

1. The most frequent positions are longitudinal.

2. The most frequent combinations are cephalopodalic and bicephalic.

3. The vertex presentation is much less

Table XXXII

COMBINATIONS OF MODES OF PRESENTATION OBSERVED IN TWIN PAIRS (%)

Presentation	*Cazeaux*	*Depaul*	*Bar*	*Rouzaud*	*Tauber*	*Werth*	*Leonhard*	*Favreau & Beurois*	*Takahashi*	*Gernez & Omez*	*Somaglia*
Cephalic in both twins	47	46.7	38	46.7	31.4	47.4	38.5	48	42.5	42.0	35.2
Cephalic in one twin, breech in the other	33.5	39.5	31.5	31.5	38.2	34.2	47.2	37.0	49.3	42.5	40
Breech in both twins	11	20.9	8.9	9.3	12.3	8.4	10.8	4	6.1	8	9
Cephalic in one twin, transverse position in the other	0.8	7	7.5	8.5	10.1	5.8	9.2	2	1.7	7	3
Breech in one twin, transverse position in the other	0.4	1.4	2.6	4	6.7	3.6	5.1	6	0.4	0.5	3
Both twins in transverse position	0	0.7	0.7	0	1.1	0.47	0.9	0	0	0	0.5

common in twins than it is in a single pregnancy.

4. The various positions assumed in vertex and breech presentations occur with about the same frequency in twins as in single pregnancies.

COMPLICATIONS OF TWIN PREGNANCY

A prompt diagnosis of multiple pregnancy is essential for both doctor and mother, so that they may be prepared for this difficult type of pregnancy. Complications in gemelliparity are rather common, and may be maternal or ovular in nature. According to Somaglia, they occur in 63.96% of the cases. The most frequent maternal complications are albuminuria, eclampsia and circulatory disturbances. Other complications are polyhydramnios, abortion, premature birth, hydatidiform mole formations, papyraceous degeneration

Table XXXIII

DISTRIBUTION OF LIVE BIRTHS AND STILLBIRTHS IN TWINS, ACCORDING TO MATERNAL AGE (FRANCE, 1907-1910, WITH THE USE OF WEINBERG'S DIFFERENTIAL METHOD), AS REPORTED BY DAHLBERG

	Age of Mother						*Total**	
	15-19	20-24	25-29	30-34	35-39	40-44		
Births (number of mothers)	175,131	868,208	925,078	658,465	385,721	143,982	3,218,547	Group I
Twin births	977	6,638	9,500	7,031	2,127	2,127	36,653	
Percent	0.56	0.76	1.07	1.44	1.82	1.48	1.14	
Opposite-sex pairs	217	1,964	3,396	3,504	2,774	804	12,818	
Percentage of Dizygotics	0.25	0.45	0.73	1.06	1.44	1.12	0.80	
Percentage of Monozygotics	0.31	0.31	0.34	0.38	0.38	0.36	0.34	
Stillbirths (single births plus twin births with both dead)	7,354	32,323	35,237	28,566	20,443	9,690	140,022	Group II
Stillborn pairs with both dead	150	628	718	566	369	146	2,639	
Percent	2.04	1.94	2.04	1.98	1.81	1.51	1.88	
Opposite-sex pairs	31	144	180	167	108	37	685	
Percentage of Dizygotics	0.84	0.89	1.02	1.17	1.06	0.76	0.98	
Percentage of Monozygotics	1.20	1.05	1.02	0.81	0.75	0.75	0.90	
Stillbirths (single births plus twin births with one or both dead)	7,468	33,050	36,211	29,459	21,163	9,950	143,747	Group III
Stillborn pairs with one or both dead	264	1,355	1,692	1,459	1,089	406	6,364	
Percent	3.54	4.10	4.67	4.95	5.15	4.08	4.43	
Opposite-sex pairs	51	349	501	459	370	133	1,893	
Percentage of Dizygotics	1.36	2.11	2.77	3.12	3.50	2.67	2.63	
Percentage of Monozygotics	2.18	1.99	1.90	1.65	1.65	1.41	1.80	
Live births with at least one alive	167,777	835,885	889,841	629,899	365,278	134,292	3,078,525	Group IV
Pairs with both twins live-born	713	5,283	8,225	8,041	5,941	1,721	30,289	
Percent	0.42	0.63	0.92	1.28	1.63	1.28	0.98	
Opposite-sex pairs	166	1,615	2,895	3,045	2,404	681	10,925	
Percentage of Dizygotics	0.20	0.39	0.65	0.97	1.32	1.01	0.71	
Percentage of Monozygotics	0.22	0.24	0.27	0.31	0.31	0.27	0.27	

*Including births by mothers of unknown age.

of one twin, stillbirth.

The following figures on infant mortality in twins have been reported by Italian authors: Viana 34%, Lanzara 37.2%, Fabris 39.7%, Floris 18.3%, Vaccari (for fetal mortality during labor and delivery) 7.54%, Somaglia 22% (13% for stillbirth and 9% for infant mortality). The effect of premature birth on infant mortality was demonstrated by Somaglia with the finding that of 64 stillborn twins, 52 were premature. Accordingly, about 85% of stillbirths in twins may be assumed to be determined by prematurity.

In Japan, the mortality rate in twins, up to the seventh day from birth, was reported by Takahashi to be 13.7%.

In line with figures supplied by Dahlberg (Sweden, 1891-1910), the rate of stillborn twins (pairs with one or two dead) was 7.7% of all stillbirths (stillborn single births plus twin births with one or two dead). This rate, much higher than the frequency with which twin births occur in the population, reflects the danger of stillbirth in twin pregnancies.

Dahlberg made another analysis of stillbirths, based on French statistics for the years 1907-1910. The tabulated data (Table XXXIII) show that among the stillborn (Group III) the percentage of twins rises with increasing maternal age (though not so rapidly as it does among the live-born) and reaches its peak at 25 to 39 years. The same table reveals that twin births represent 4.43% of the stillborn (Group III), but only 0.98% of the live-born (Group IV). Inclusion of the stillborn would cause an increase of the twin birth percentage to 1.14 (Group I).

As to zygosity differences in stillbirths, it is of interest that living MZ twins represent 0.27% of the live-born, and stillborn MZ twins, 1.80% of the stillbirths. Hence the frequency of MZ stillbirths is six to seven times that of the live rate. By contrast, DZ twins represent 0.71% of all living children and 2.63% of all stillbirths. In other words, the frequency of stillborn DZ twins is three to four times that of living DZ twins. These differences seem to prove the assumption that the danger of stillbirth is higher for monochorionic than for dichorial twins.

In the United States, Yerushalmy and Sheear (1940) found 572 stillbirths in a series of 1,253 twin births, that is, a threefold increase over natimortality in single births. In Japan, Araki (1933) observed a 9% rate of twin stillbirths, as against a 5% rate in single pregnancies.

Differential stillbirth statistics (single and twin deliveries) were compiled by Strandskov and Ondina (1947) for white and nonwhite populations in the United States from Bureau of Census figures for 15 consecutive years (1922-1936). The analysis was complicated by the fact that the different states followed different rules of registering deaths that occurred in the early stages of fetal development. Some states included only stillbirths at or near term, and some recorded no stillbirths whatever. According to the authors, however, these discrepancies were evenly distributed over the material as far as single and twin births were concerned.

Limiting our review to data on the two sexes and white and nonwhite population, we find that the percentage of stillbirths was 3.504 for single births, 7.533 for twin births, 14.281 for triplet births, and 19.922 for quadruplet births. The differences between single and twin stillbirths and between those of twins and triplets were statistically significant, while that between triplets and quadruplets approached statistical significance. Therefore, the authors concluded that the percentage of stillbirths in the total population of the United States showed a significant increase with the increase in number of embryos in the pregnancy.

The causal factors mentioned included premature birth, mutual interference of fetuses, double malformations, maternal toxemia, and the like. Moreover, natal mortality appeared to be higher in males than in females, both in single and multiple births, with the difference attributed to genetic factors. It was also found increased in nonwhite groups. This difference was ascribed chiefly to environmental factors, although some genetic influence was not entirely ruled out.

In addition to Dahlberg's data on the frequency of stillbirth, there are French statistics compiled by Turpin and Caratzali (1937) for the period 1928 to 1930. The following comments were made by the authors regarding the figures presented in Table XXXIV: "A series of pregnancies makes the uterus more extendable, and thus better suited to contain two embryos, whether they are MZ or DZ. However, this advantage is lost when the mother passes her fortieth year of age. At this time the uterine tissue reaches a stage of involution."

As often happens in the study of twins, mortality data pertaining to multiple births have far-reaching implications. Using one of March's tables from *Statistique Internationale* (reproduced in Table XXXV), Apert made a number of interesting observations. As opposite-sex twins are always dichorial, monochorionic twins may be assumed to be more susceptible to lethal factors than dichorial pairs. For this reason alone, it would seem essential that a distinction be made between the two types of twins.

Regarding the greater resistance of the

Table XXXIV

RATE OF STILLBIRTHS (%) IN RELATION TO MATERNAL AGE (TURPIN AND CARATZALI)

Percentage of Stillbirths	*Age of Mother*					
	-20	20-24	25-29	30-34	35-39	40+
All births	3.27	2.79	2.95	3.59	4.55	6.39
Opposite-sex Twins	12.58	8.39	6.77	6.30	5.90	7.35
Same-sex Twins	22.56	11.15	8.50	7.68	9.06	9.56

Table XXXV

SEX DIFFERENCES IN TWIN MORTALITY DATA (MARCH)

		Male Deaths		*Female Deaths*	
		Male Pairs	*Opposite-sex Pairs*	*Opposite-sex Pairs*	*Female Pairs*
France	1902-1906	1,074	998	929	874
France	1907-1910	1,510	1,066	945	1,176
Holland	1903-1906	1,171	776	721	721
Norway	1886-1900	779	533	520	643
Sweden	1871-1905	1,054	772	671	871
Austria	1896-1905	784	573	503	658
Hungary	1900-1905	684	505	505	563
Saxony	1881-1890	831	556	556	700

female, which typifies statistics on general natal mortality, this phenomenon was found to apply to twins to the same extent as to nontwins. According to Apert, lower mortality in females is generally attributed to the fact that they are smaller at birth, thus making the delivery easier. In the case of twins, the males are also small, so this explanation is no longer plausible. It should therefore be admitted, although this rather upsets many common ideas, that the male sex is more fragile than the female, the latter being "the stronger sex." Tables of mortality at different ages actually show that this inferiority of the male sex in regard to disease and death remains not only during childhood but actually for the whole course of the subjects' life and for nearly all diseases.

ECTOPIC TWIN PREGNANCIES

Twin pregnancies may be divided into *uterine* and *extrauterine* or ectopic ones, according to their site. With respect to the latter type, Werth's classification (1888) distinguishes three different forms: (1) One embryo develops in the uterus and the other outside the uterus. (2) Both embryos develop in the same Fallopian tube. (3) The embryos develop in different tubes.

This classification was criticized by Sawitzky, since in the first case, strictly speaking, one cannot refer to a multiple extrauterine pregnancy, but only to a combined intra- and extrauterine pregnancy. The Russian author therefore suggested limiting the classification of authentic extrauterine multiple pregnancies to two groups.

According to Christitch, extrauterine twin pregnancies may be divided into tubal and bitubal, in addition to a third group combining intra- and extrauterine pregnancies. The second group would be much more frequent than the first.

The outcome of an extrauterine twin pregnancy is always an unfortunate one for the twins and extremely dangerous for the mother. That she may survive has been shown by a case of Ferguson and Otis. When the woman was operated upon 12 months after cessation of menstruation, a twin pregnancy was found in the left Fallopian tube, with both dead twins having reached approximately the seventh month of development. In a case described by Sawitzky, two monochorionic biamniotic twins, 12 cm. in length, were found in the right tube. The diagnosis of extrauterine twin pregnancy had been made in the fourth month, and the woman survived after salpingectomy.

Mention may be made here of a phenomenon which, though extremely rare, has been described in the obstetrical literature. This is the occurrence of a twin pregnancy in a uterus bicornis. In 1925 Rowlett reported the case of a double uterus with a pregnancy in each horn. The presence of such an abnormality had been established two years before by laparatomy. After a pregnancy of five months, the woman gave birth to two male fetuses weighing 1,420 gm. and 990 gm.

In 1929 Costantini described the history of a woman who had brought all her pregnancies to term with spontaneous delivery, always showing at the right of the uterus a tumor which had been diagnosed as an ovarian cyst. When pregnant for the seventh time, she consulted a surgeon because the old tumor had grown rapidly. Upon opening the abdomen two symmetrical uteri were found, both of them pregnant. Similar cases were placed on record by Barrett (1934), Johnston (1939), Braze (1943), Brody (1954) and others.

GENERAL OBSERVATIONS

The physiologic and pathologic aspects of the delivery of twins may be briefly reviewed as follows: Such a delivery is quite different from that of a single fetus, not only because it can be considered as a sequence of two single deliveries, but also because of other characteristics which compare favorably or unfavorably with ordinary pregnancies.

One advantage of a twin delivery lies in the relative size of the infants, which is generally smaller than in single children and facilitates passage through the genital canal. Although similar conditions are found in premature single births, the difference is that twins who have normally reached term are favored by the presence of a uterus which has reached the same stage and, therefore, possesses full expulsive and hemostatic capacity.

In consequence, the twin fetuses sustain less damage when passing through the hard and soft parts of the genital canal. On the other hand, uterine contractions tend to be less energetic, since the muscular fibers of the uterus are notably distended. In this respect the benefits of small-sized fetuses and a more distended uterus are somewhat diminished. Moreover, the first twin has the disadvantage of leaving a non-contracted uterus, with contractions being transmitted indirectly through the second fetus and its membranes. According to Gasparri, it is especially during the third period of labor, i.e. rotation, that the first twin is hampered by the presence of the other.

In Borsò's opinion, the second twin is in a more favorable position since he finds the passage clear and wide. Of course, there is the disadvantage of leaving a large mass of contracted uterus behind. This complication may cause ischemia of the placenta and lead to asphyxia in the fetus, if delivery does not follow the interval of rest as soon as the expulsive contractions of the uterus are renewed.

Although Revoltella believed that a twin delivery is easier than a single birth, largely from a mechanical point of view, such a contention needs to be modified. There are other complications that may aggravate the period of labor, parturition and afterbirth. Because of its size, the placenta is often found to be a placenta previa and may cause severe hemorrhages, or it may detach itself. Other complications affect the uterus, which, contracting with greater difficulty than in single pregnancies, may show a primary inertia lasting as long as six hours. According to Favreau and Beurois, this condition occurs in 20% of the cases.

At any rate, labor pains tend to be protracted, and the periods of dilatation and expulsion lengthened, thus inviting danger. Also, the uterus may be affected by secondary inertia, with consequent diminution of its hemostatic power complicating the afterbirth of a twin pregnancy, as compared with that of a single one. In addition, membranes and blood clots are more likely to be retained, so that infections set in.

Other complications may arise from abnormal presentations which are more frequent in the second twin. The reason is a certain disproportion between the uterine cavity and its contents, which can move more freely. However, with Hergott one may point to the case of a mother who, after the normal delivery of one twin at home, was removed to a hospital because the second twin was in a transverse presentation. When she reached the hospital, after two hours of travel, the child was born, weighing 3,200 gm.

The abnormal positions of the fetuses in the uterus may result in a simultaneous penetration of both heads into the pelvis, as in a case described by Mahnert (1922). Usually, there is a locking of the twins when the two heads appear together (Fig. 110). Such a case was reported by Balard (1923), with the first a breech and the sec-

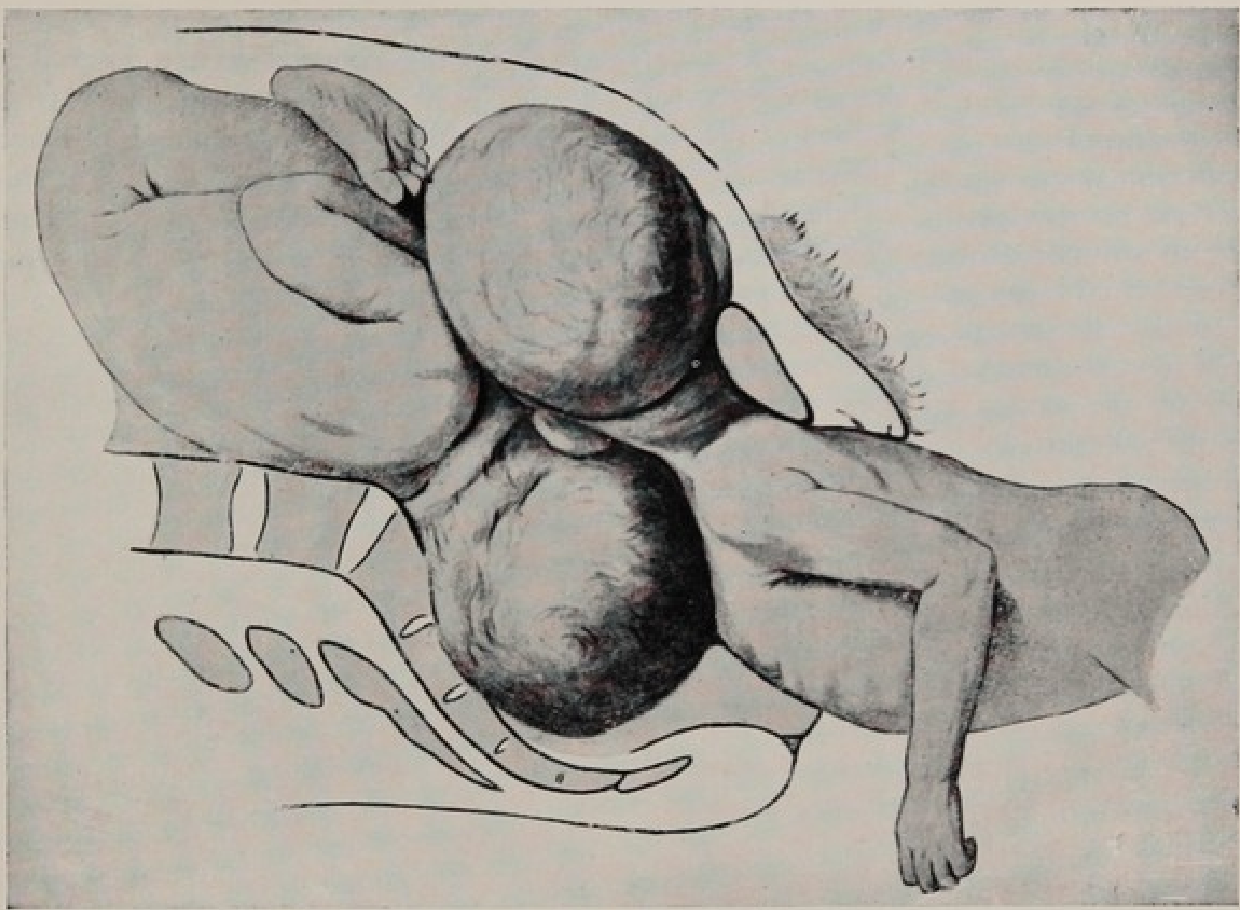


Fig. 110. Fetal dystocia due to locking of heads (Hoehne).

ond a vertex. More frequently, the locking takes place between the head of the first, which is the last to be delivered, and the head of the second, which comes first. A case of this type was presented by Couvelaire (1905).

The expulsion of the first fetus requires the cutting of the corresponding umbilical cord as well as two ligatures, in order to avoid a rupture in the cotwin's circulation. The expulsion of the first child is followed by a pause, during which the uterus ceases to contract before renewing its expulsive effort. Whenever possible it is inadvisable to interfere with this period of uterine rest.

The average duration of the pause, as estimated by Vaccori from 138 cases, is 19 minutes. The given figures show that the pause lasts longer in primiparae (average time 23 minutes) than in multiparae (average time 18 minutes). Other investigators supplied the following figures: Ribemont-Desaignes 10 to 12 minutes, Tarnier (188 cases) 15 to 20 minutes, Favreau and Beurois 20 minutes.

From a more detailed analysis (see below), Gernez and Omez concluded that the interval between expulsions is less than 15 minutes in 62% of the cases, regarding this time lag as the norm:

Interval Between Expulsion of the First and Second Twin (Gernez and Omez)

(minutes)	*(cases)*
1 to 5	43
6 to 10	35
11 to 15	31
16 to 30	25
31 to 60	23
61 to 120	10
121 or more (including one interval of 10 hours)	9

When the uterus' rest is prolonged, the pregnancy is extended for the second twin, creating a condition of danger mostly for the mother. When the expulsion of the second twin does not take place within two or three hours, obstetricians advise proceeding to artificial delivery. The birth of the second child is not preceded by a period of dilatation. In normal cases after the pause, that is, at the onset of the second expulsive period, the second sac appears and ordinarily is broken by instrument. Should the presentation of the fetus warrant it, advantage may be taken of the interval in order to perform an external version. This maneuver puts the second child in a position of advantage over the first, because of its smallness, the absence of contractions, and the wide space of the uterine cavity. Resumption of the expulsive period completes the delivery, after which, ordinarily, the fetal membranes are expelled.

As to the most frequent hour for twin deliveries, v. Verschuer (1932) reported that while most single births take place during the three hours after midnight, the majority of twin births occur around noon.

Chapter IX

ANATOMICAL STUDIES OF TWINS

It is hoped that this part of the book will help to open new roads for objective approaches to the genetic aspects of anatomy.

While the aim of this research modality is twofold, relating at the same time to twins and to human biology in general, the investigative procedure is fundamentally the same. Whatever the objective, the method calls for a comparison of two twin partners with a complex interplay of endogenous or exogenous factors responsible for their various degrees of similarity. The assessment of a given degree of similarity—its extent, meaning and specific ramifications—is the purpose of this comprehensive review of the numerous investigations based on the study of twins.

All of the studies that have been conducted with a view to exploring a particular scientific area require first an intra-pair comparison (between twin partners) and then an interpair comparison (between groups of MZ and DZ pairs). In order to make such double comparisons possible, the first step must be zygosity diagnosis, followed by the intra-pair comparison and then an interpair analysis of representative group samples. While the intra-pair comparison may be anthropological or clinical, it is always effected on the twins themselves. The interpair comparison is made statistically and effected on the data obtained from two comparable samples of MZ and DZ pairs.

Even when considered by itself, an intra-pair comparison can yield important results. In an MZ pair, for instance, useful information may be secured in the genetic field (regarding the penetrance or expressivity of genes), as well as for clinical purposes, as in cases of different degrees of similarity in innate factors, or complete discordance as to externally conditioned diseases. When the genetic or nongenetic nature of any given normal or pathological trait is to be established, or a combination of the two sets of etiological factors, comparison between the two groups of twins is necessary, owing to their hereditary differences.

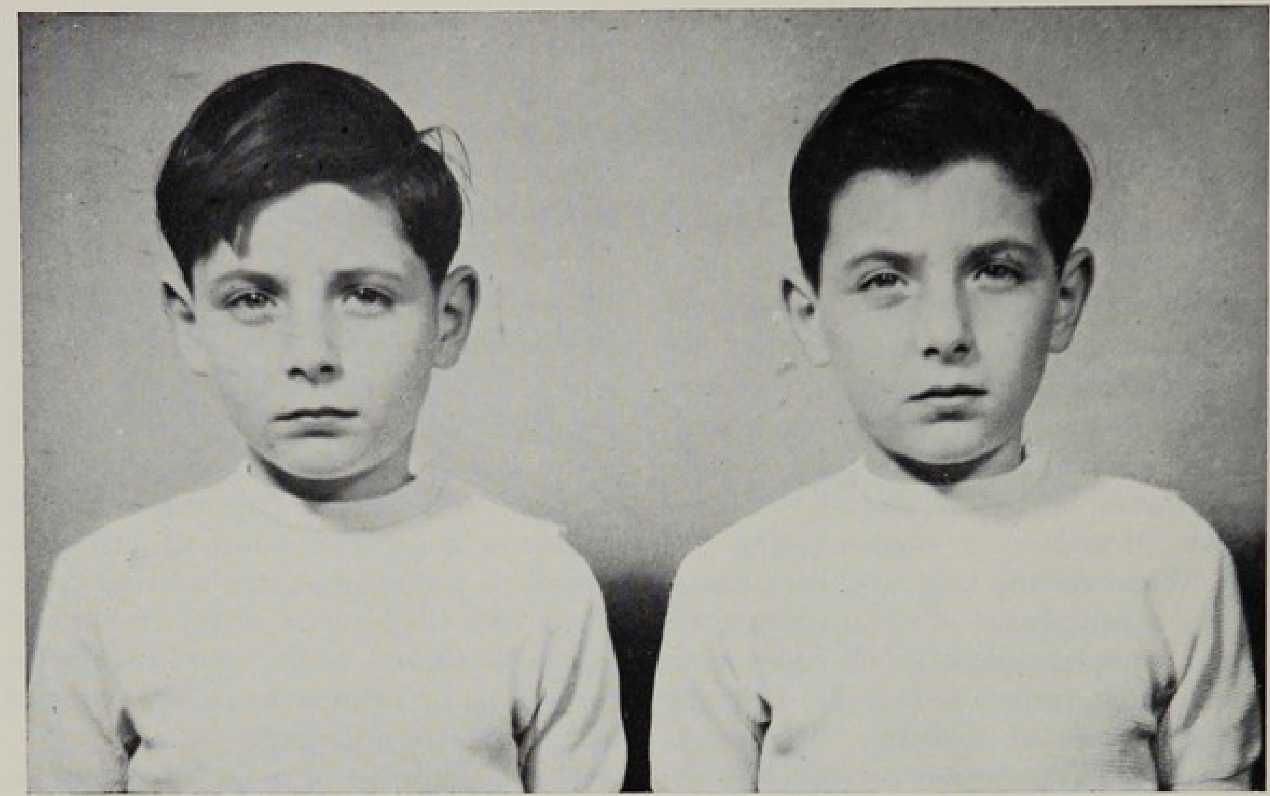
The investigation of twins has many other facets, among them being the requirement of unselected and statistically representative samples, the comparison of same-sex and opposite-sex DZ twins, the statistical analysis of the data obtained, and the like. The following section will illustrate the various methodological aspects of twin studies.

A wider analysis of the methodology of twin research may be found in the last chapter of the second volume of the present work, while authoritative contributions on the subject have been made by various authors in recent years (Kallmann, 1953, 1954; Waardenburg, 1957; Walker, 1957).

The various aspects of anatomy and morphology have been investigated over a period of more than 30 years by a number of Japanese researchers using as material a number of twin fetuses (Taniguchi, 1955).

1. ANECDOTAL MATERIAL

The pronounced similarity of MZ twins (Figs. 111 and 112) and the comparative



Figs. 111 and 112. Similar facial features in MZ twins (Gedda).

Figs. 113 and 114. Marked disparity in height in DZ twins (Gedda).

dissimilarities between DZ partners (Figs. 113 and 114) have attracted the attention of many scholars. The similarity of MZ twins, as we have noted, has been widely exploited in art and literature. In everyday life, it is not only helpful to science but it gives rise to many a comedy of errors.

Galton described one instance as follows: "An artist who had been commissioned to paint the portrait of two twins, three to four years of age, put his work aside for a few days, and on taking it up again was not able to remember which portrait belonged to which child."

Of another case Galton wrote, "Two twin girls used to trick their music teacher when they wanted to get some free time. Since their lessons were fixed at different times, one of them made the sacrifice of having two lessons on the same day, so that the other was able to enjoy herself all day long."

The daughter of one of these twins gave Galton a personal account of her mother and aunt. "Their physical appearance, their voices and mannerisms showed such a remarkable resemblance," she said, "that I remember being very embarrassed about it as a child. Had my aunt lived with us, I would have had two mothers."

Such occurrences are common in the histories of MZ twins. Here, for example, are some anecdotes reported originally by Newman, Freeman and Holzinger (1936) and later recounted by Caullery:

Ed and *Fred* were adopted by different families and lived 150 miles apart. When he was 22 years old, Ed went to Chicago and there was greeted on the street by a total stranger who called him Fred. Ed paid no attention at first, but the stranger persisted, thinking he was addressing the other twin. This chance encounter brought the long-separated twins together again.

Eleonora and *Georgiana* were also separated at an early age and were unaware of each other's existence. Boarding a bus one day, Eleonora met a nun who mistook her for the twin who was one of her pupils. In this manner the girls found each other.

While *Helen*, a school teacher, was aware that she had a twin sister *Gladys*, she had never met her. Then one day Helen found herself reproached by one of her favorite students for ignoring her smile of greeting at a movie theatre. Of course, it had really been Gladys and the incident led to the reunion of the twins.

A friend of ours, a well-known *surgeon*, had an *ordained* twin brother who lived in the same town. The surgeon was often teased by his colleagues. "What's the idea," they would cry, "trying to pass yourself off in public as a priest?"

According to Guttmacher, mothers of MZ twins are not the only ones who have trouble telling them apart. Even dogs, despite their highly developed sense of smell, get confused about who their master is if he happens to have an identical twin.

These vignettes, in Poyer's opinion, are not without scientific interest. As a matter of fact, some one-egg twins resemble each other so greatly, that it is difficult by any scientific procedure to measure with precision their extraordinary degrees of similarity.

2. BIOMETRIC DATA

In 1925, Scheidt examined seven MZ pairs, three DZ pairs, and three pairs of undetermined zygosity. In general, the intrapair differences in one-egg twins were significantly smaller than those in two-egg twins, although it was clear that the zygosity diagnosis could not be based on biometric measurements alone.

In the same year, v. Verschuer reported on 42 MZ pairs from Thuringia, with measurements on stature, length and breadth of the head, length of the arms, trunk and lower limbs, facial and various other diameters, and the like. The average intra-pair differences in MZ twins were remarkably low, as was the probable error of the given data. It also was of interest that in a younger group of twins the observed deviation was .75±.12% and in an older group .79±.3%, a small but apparently not insignificant difference.

One year later (1926), Dahlberg presented data on 243 Swedish twin pairs, with careful tabulations of 15 different measurements (Table XXXVI). The measurements were taken by two investigators, and repeated control measurements on the same persons revealed differences ranging from .5 to 1.5 mm. for the cephalic circumference, and from 3 to 7 mm. for height. The smaller intra-pair differences in MZ twins are graphically shown for head length in Figure 115.

Comparable measurements were obtained by Dahlberg for four groups of 100 pairs each: one-egg twins, same-sex and opposite-sex two-egg twins, and two full sibs in military service, measured at different times, when each had approximately 21 years of age. The tabulated data showed the smallest intra-pair differences for every single measurement in MZ twins, and the highest in DZ twins of opposite sex (Table XXXVI). By and large, same-sex DZ twins yielded the same mean intra-pair differences as two brothers examined at a comparable age. The effect of sex differences was demonstrated most clearly by the average of the averages, which varied from 8.22 mm. in MZ twins, to 19.59 in brothers, 19.82 in same-sex DZ twins and 23.75 in opposite-sex DZ twins.

Some years later, Dahlberg computed the sums of the per mil values for each measurement and obtained the lowest figures in MZ twins (211.58 ± 9.27‰), the highest in opposite-sex DZ pairs (594.37 ± 38.72‰), and intermediate values in same-sex DZ pairs (496.09 ± 18.6‰). Accordingly, twins with a total anthropometric difference of less than 300 per mil proved to be monozygotic in 86.4 per cent of the MZ group,

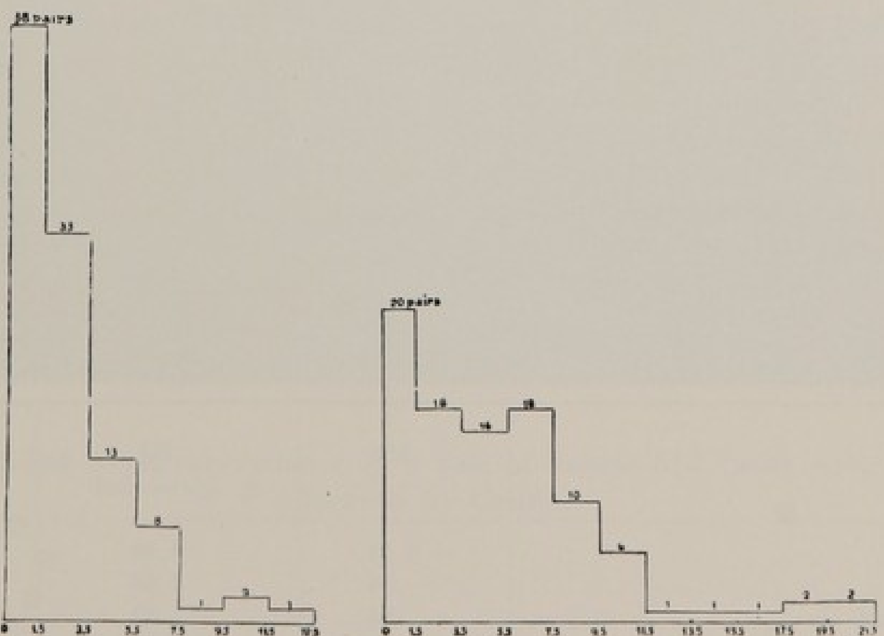


Fig. 115. Intra-pair head length differences (in mm.) in MZ (left) and DZ (right) twins (Dahlberg).

Table XXXVI
MEAN INTRA-PAIR DIFFERENCES IN ANTHROPOMETRIC MEASUREMENTS, AND THEIR STANDARD ERRORS (DAHLBERG)

	MZ	*DZ (same sex)*	*Brothers (non-twins)*	*DZ (opposite sex)*
Length of head	2.57±0.20	5.42±0.42	5.32±0.37	7.10±0.74
Width of head	1.74±0.13	3.95±0.31	4.09±0.29	5.15±0.54
Minimum frontal diameter	1.55±0.12	7.73±0.29	3.55±0.23	4.02±0.42
Width of face	1.59±0.12	3.53±0.27	3.91±0.27	5.17±0.54
Bigonial diameter	1.56±0.12	3.82±0.30	4.15±0.29	3.35±0.46
Length of face	2.46±0.19	4.26±0.33	5.39±0.38	4.79±0.61
Stature	16.27±1.28	50.66±4.01	46.77±3.27	57.60±6.41
Length of sternum	14.65±1.19	44.20±3.54	40.91±2.86	50.71±5.91
Height of symphysis	11.23±0.94	35.53±2.86	32.63±2.28	40.12±4.68
Height of acromion	17.69±1.43	44.00±3.52	43.62±3.05	52.00±6.06
Height of tip of middle finger	14.48±1.17	27.93±2.24	25.96±1.81	29.52±3.44
Length of arm	10.76±0.87	25.27±2.02	28.21±1.97	37.24±4.34
Length of trunk	14.60±1.23	21.32±1.72	22.57±1.58	25.36±2.96
Biacromial diameter	6.44±0.52	13.21±1.06	14.42±1.01	18.60±2.17
Bicrestoiliac diameter	5.64±0.46	10.53±0.85	12.50±0.87	13.54±1.60
Average of the averages	8.22 —	19.82 —	19.59 —	23.75 —

while 90% of DZ twins showed differences of more than 300 per mil. In other words, close physical similarity as demonstrated by anthropometric measurements goes with genotypical identicalness of one-egg twins, and gross dissimilarity with the nonidenticalness of two-egg twins.

In later biometric studies (1927-1931), v. Verschuer computed the percentage deviation for single pairs, and the mean percentage deviation (E) for a series of pairs to express the degrees of intra-pair similarity (see chapter on Methodology, Vol. II). The results obtained by this method in the three groups of twins agreed closely with Dahlberg's data (Table XXXVII).

Interpair differences in mean percentage deviation (E) were graphically presented by v. Verschuer with respect to both height (Fig. 116a) and length of head (Fig. 116b). In MZ twins, the variability curve for height is parabolic. Its highest point is at 0, since intra-pair differences are generally small. In DZ twins of the same or opposite sex, the curve is flattened and its peak is not at 0.

Table XXXVII
MEAN PERCENTAGE DEVIATIONS (ϵ) IN BIOMETRIC MEASUREMENTS (v. VERSCHUER)

	MZ	*DZ (Same-Sex)*	*DZ (Opposite-Sex)*
Body weight	2.24	4.89	6.53
Height	.54	1.63	2.04
Length of the head	.84	1.52	1.92
Width of the head	.79	1.39	2.96
Bizygomatic diameter	.71	1.37	—

Plate III. Marked facial concordance in a pair of female MZ twins 10½ years of age (observed by Gedda).

Plate IV. Marked facial concordance in a pair of female MZ twins 11 years of age (observed by Gedda).

Plate V. DZ twins 10 years of age (observed by Gedda).

Plate VI. A pair of DZ twins of opposite sex, 11 years of age (observed by Gedda).

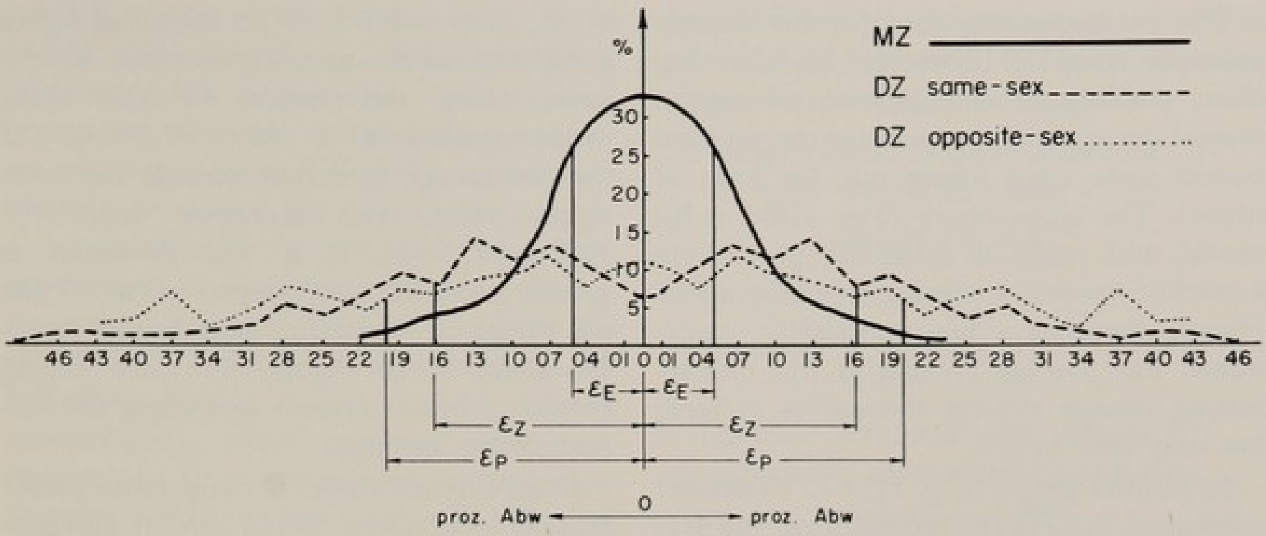


Fig. 116a. Interpair differences in mean percentage deviation (proz. Abw.) as to height (v. Verschuer).

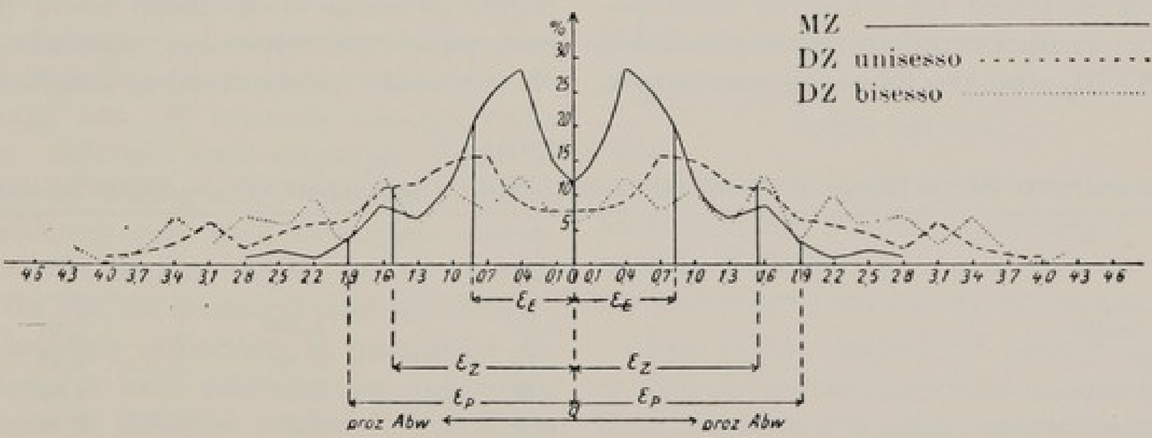


Fig. 116b. Interpair differences in mean percentage deviation (proz. Abw.) as to antero-posterior cephalic diameter (v. Verschuer). Unisesso=same-sex. Bisesso=opposite-sex.

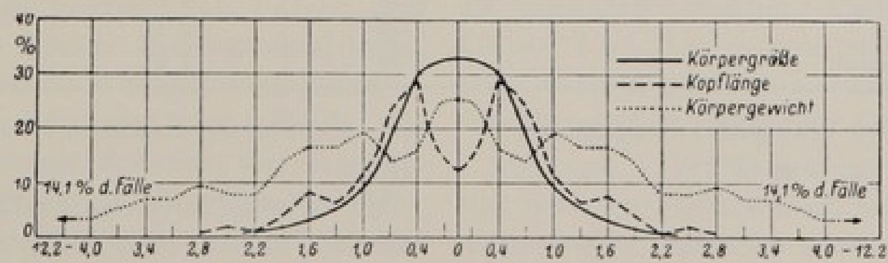


Fig. 117. Mean percentage differences in height (*Körpergrösse*), antero-posterior cephalic diameter (*Kopflänge*), and body weight (*Körpergewicht*), all for MZ twins (v. Verschuer).

The corresponding data for the antero-posterior cephalic diameter are far less clear, possibly as an indication of uneven cranial development in twins in the prenatal period (one twin losing out for lack of space). The given curve (Fig. 116b) is bimodal, with peaks on either side of 0 where a marked depression appears. It may be inferred, therefore, that genetically determined interpair differences in this characteristic cannot express themselves at birth but only later in life.

In another graph (Fig. 117) v. Verschuer compared the curves representing the frequency of average percentage deviation in height, weight and cephalic diameter in a representative sample of 450 MZ pairs of either sex. The sigma values of the frequency curves traced for the given anthropometric measurements are shown in Table XXXVIII, with the following percentages, encompassed by multiples of sigma (σ):

$$\pm\ \sigma = 68.3\%$$
$$\pm\ 2\sigma = 95.5\%$$
$$\pm\ 3\sigma = 99.7\%$$

In computing the percentage deviation of a measurement, the chances of a pair's being monozygotic can be assumed to be as low as .3% ($100 - 99.7 = .3$), if the given figure is higher than the three-sigma value. By the same token, the chances of their being monozygotic is 4.5% ($100 - 95.5 = 4.5$), if the percentage deviation exceeds the two-sigma value, and increases to 31.7% ($100 - 68.3 = 31.7$), if the deviation is greater than the single-sigma value. While the range of variability was found by v. Verschuer to be slightly increased during puberty, there were no significant sex differences at any age.

In an English study of twins from public schools in London, Stocks (1930) computed the following biometric measurements for a total of 832 individuals including 386 members of the same-sex and 176 members of opposite-sex twin pairs: height, weight, degree of facial resemblance, blood pressure, pulse rate, respiration, measurements of the head (circumference, longitudinal and transverse diameters), and bi-ocular width.

MZ twins in early childhood tended to be taller and heavier than DZ twins of the same age, with their single born sibs somewhere between the two groups with respect to height but not with respect to weight (sibs

Table XXXVIII
STANDARD DEVIATIONS OF CERTAIN BIOMETRIC MEASUREMENTS (v. VERSCHUER)

	1σ	2σ	3σ
Body weight	2.65	5.30	7.95
Height	.75	1.50	2.25
Length of trunk	1.62	3.24	4.86
Biacromial diameter	1.29	2.58	3.87
Biiliac diameter	1.62	3.24	4.86
Thoracic circumference	1.55	3.10	4.65
Breadth of thorax	1.85	3.70	5.55
Longitudinal diameter of thorax	2.4	4.8	7.2
Circumference of head	.94	1.88	2.82
Length of head	1.20	2.40	3.60
Breadth of head	1.18	2.36	3.54
Height of face	1.23	2.46	3.69
Bizygomatic diameter	1.14	2.28	3.42

generally being on the heavier side). As to cranial development, too, DZ twins were inferior to MZ twins, while there was no intergroup difference either between same-sex and opposite-sex DZ twins or between two-egg twins and sibs of the same age.

An appraisal of the interaction of genetic and nongenetic factors in producing the various characteristics measured showed a decline in the contributions of heredity in the following order: height, weight, cranial measurements, blood pressure, pulse rate, respiration. In a subsequent investigation (Stocks, 1933), it was confirmed with respect to height, weight and cranial diameters that MZ twins show the highest degrees of intra-pair similarity.

Comparable biometric studies by Csik and Apor in Hungary (1937), using v. Verschuer's method of computing the percentage deviation, were concerned with 130 one-egg and 160 same-sex two-egg twins from different socio-economic levels in Budapest, ranging in age from 5 to 42 years. Considering only such measurable characteristics as height, weight, size of thyroid, and the like, the investigators observed varying interpair differences in percentage deviation for each measurement, apparently because of different modes of interaction between genetic and environmental influences. The characteristic with the highest genetic component was stature.

In order to appraise the effect of age on these values, the twin sample was divided into three age groups: 5-12, 13-17, and 18-42. In this manner environmental influences on variations in height were found to decline with increasing age. While the smallest percentage deviation was obtained in the oldest group of MZ twins, the highest value was computed in male MZ adolescents (second age group).

In a study dealing primarily with vital capacity variation, Werner (1938) also compiled data on various somatic indices in a series of 35 MZ and 25 DZ pairs of twins, using the following procedures:

1. Rohrer's index of body structure:

$$\frac{\text{body weight in grams} \times 100}{\text{height (in cm.)}^3}$$

2. Kaup's index (Quételet):

$$\frac{\text{body weight in grams}}{\text{height (in cm.)}^2}$$

3. Thoracic circumference (Brugsch):

$$\frac{\text{expiratory circumference of thorax (in cm.)} \times 100}{\text{height (in cm.)}}$$

4. Thoracic expansion index (Brugsch):

$$\frac{\text{expiratory circumference (in cm.)} \times 100}{\text{inspiratory circumference (in cm.)}}$$

5. Index of interscapulary width:

$$\frac{\text{interscapulary width (in cm.)} \times 100}{\text{height (in cm.)}}$$

The results obtained by Werner are compared in Table XXXIX. According to this analysis, Rohrer's index appeared to be the one controlled most clearly by heredity.

Clark (1956) studied the heritability of 49 anthropometric characters as ascertained from measurements taken on a series of 21 female and 23 male monozygous pairs and 23 female and 14 male like-sexed dizygous pairs ranging in age from 12 to 20 years. The selection of twins, diagnosis of zygosity and program of measurements were reported separately (Sutton, Vandenberg and Clark, 1956). The greater part of the variance of most of the ascertained characters was found to be genetically determined.

Marcozzi (1957), studying the correlation between similarities of physical and of psychological traits in a series of 18 MZ and 21 DZ pairs, found that face and head measurements were significantly more similar among MZ twins, with the exception

Table XXXIX
BIOMETRIC COMPARISONS (WERNER)

	Average Differences		*Difference*	*Ratio*	*Contribution of Heredity*
	MZ	*DZ*	*DZ-MZ*	*MZ:DZ*	*(DZ:MZ)²-1*
1st Index according to Rohrer.......	.04	.15	.11	1:3.8	13.4
2nd Index according to Kaup.........	.06	.14	.08	1:2.3	4.3
3rd Index according to Brugsch......	1.3	2.3	1.0	1:1.8	2.2
4th Index according to Brugsch......	1.2	1.8	.6	1:1.5	1.3
5th Index (width between scapulae)..	.6	.8	.2	1:1.3	.7

of nose measurements. Osato and Awano (1957) reported a long series of studies carried out, in collaboration with several other researchers, on the environmental variability of a number of morphological and functional traits. One such study, on anthropometric measurements (Ito, 1948), based on data from 79 MZ, 54 same-sex and 28 opposite-sex DZ pairs, indicated that mean percentage intra-pair deviations among MZ pairs were very small where head measurements and body-length were concerned (thus demonstrating a prevalence of hereditary factors), while they were higher for body-breadth and weight (thus showing higher environmental influence). The presence of genetic conditioning for all traits was proved by the fact that differences among DZ pairs were higher than those among MZ pairs.

3. SKELETAL SYSTEM

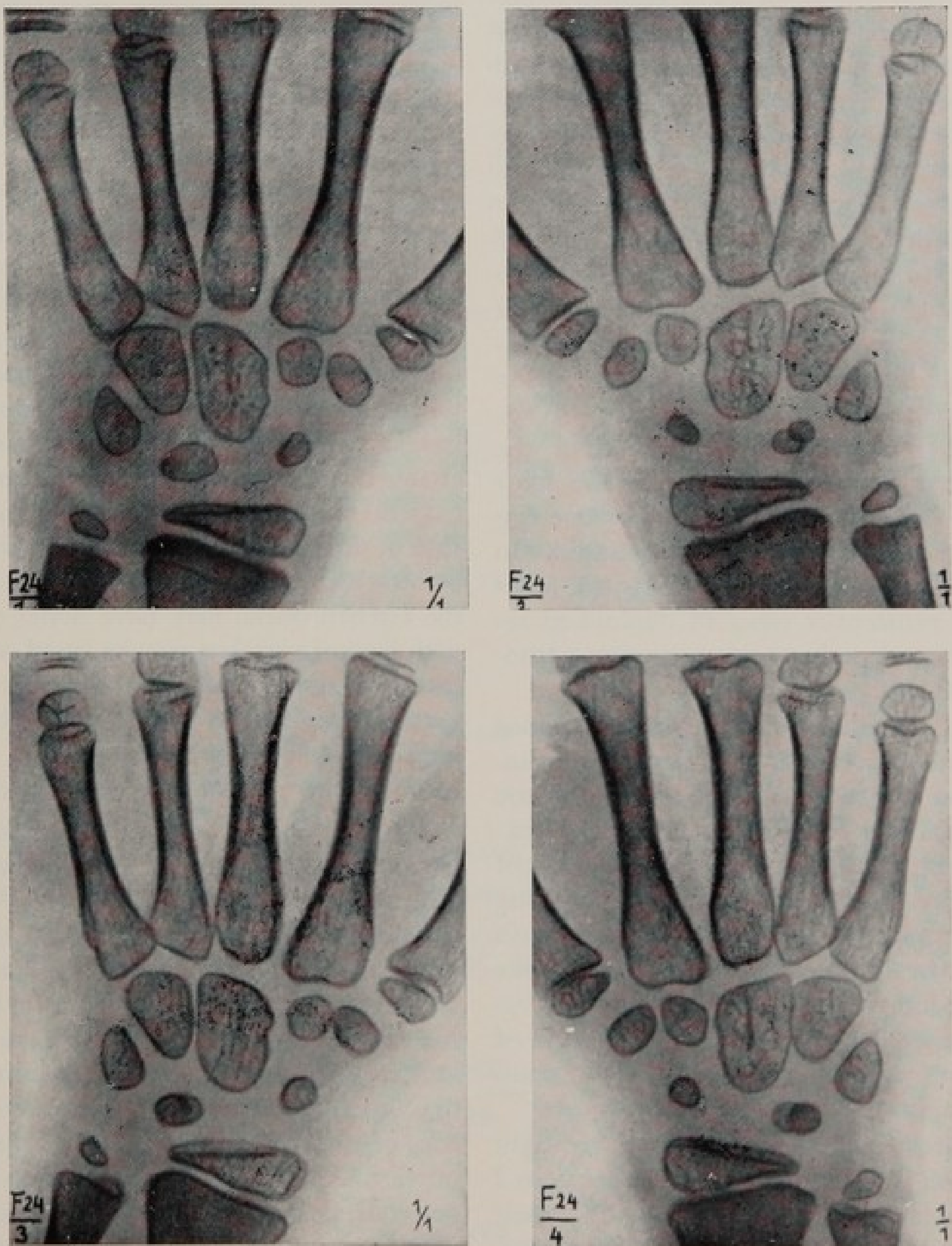
In a series of 53 MZ and 31 DZ pairs, Schwarz (1920, 1929) studied roentgenograms of the skeleton and of auditory and olfactory organs, especially sinuses and mastoid process. The frontal sinuses were found to be similar in 50% of MZ twins and in 37.5% of DZ twins; the maxillary sinus in 68.2 and 50%, respectively; and the labyrinthian portion of the ethmoid bone in 77.3 and 50% of the pairs, respectively. The nasal septum was classified as similar in 50% of MZ pairs and in 10% of DZ pairs, while the corresponding figures for roentgenograms of the mastoid process were 66.1 and 37.1%, respectively.

In a similar study of 39 one-egg pairs (Leicher, 1918), almost complete similarity in frontal sinuses was observed in 13 pairs, with only minor developmental differences in the others. Similarity in the pneumatization of the mastoid was seen in 25 MZ pairs (dissimilarity in 14 pairs), while the maxillary sinus was similar in 17 out of 18 MZ pairs and in 12 out of 18 DZ pairs, and the sphenoid sinus in 10 out of 14 MZ pairs and in 6 out of 14 DZ pairs.

Even more illuminating were the x-ray studies of Buschke (1934, 1935) and Kühne (1931). Buschke's series originally comprised 25 MZ pairs, 18 same-sex DZ pairs, 7 opposite-sex pairs, 4 sets of triplets, and 1 set of quadruplets, and was later enlarged by 1 set of female one-egg triplets examined at intervals from the age of 4½ months to 12 years. The findings showed virtually complete one-egg similarity in configuration and structure of the bones, down to the most minute details, and sizeable differences in plurizygotic subjects.

Another study by Buschke dealt with the process of ossification, especially in the bones of hands and feet. On the whole, the nuclei of ossification were found to appear at essentially the same time in one-egg twins, and only to a lesser extent in some two-egg twins. Qualitatively, too, the ossifying process was less similar in same-sex two-egg than in one-egg twins. The largest intra-pair differences were observed in opposite-sex pairs, probably because ossification progresses more rapidly in the female than in the male.

Since one-egg twins were most similar as to the time when the first series of ossifica-



Figs. 118-121. Intra-pair similarity as to the doubling of ossification nuclei in the lunate bones of female MZ twins, aged five years, with the hands of twin No. 1 (upper figures) showing separation of the two nuclei only in the right hand, and the hands of twin No. 2 (lower figures) showing the two nuclei still separated (Buschke).

tion nuclei appeared, and less similar for the second series of nuclei, Buschke assumed a higher degree of penetrance for the genes initiating the first process of ossification. Generally speaking, the twin who is ahead in growth is also the first to complete osteogenesis. What is more, rate and rhythm of ossification seem to be more definitely determined by heredity than growth in general and height in particular. In DZ twins, ossification rates may show marked similarity despite extreme differences in height.

Intra-pair similarity in the doubling of ossification nuclei is shown in Figures 118 through 121 in regard to the lunate bones of one-egg twins (Buschke). The observation that supernumerary nuclei and other osteogenetic variations (tuberosity of the fifth metatarsus, posterior process of the talus, first cuneiform bone, and the like) tend to occur in both members of one-egg pairs points to a gene-specific origin. In Buschke's opinion, they represent a *locus minoris resistentiae* (spot of diminished resistance) and perhaps a transition to pathological forms.

More specifically, Buschke concluded that bone structure is determined by an interaction of genetic (83%) and nongenetic (17%) factors. He even thought that roentgenographic comparison of hands and of feet might be a useful device for classifying one-egg and two-egg twins, since the x-rays of the former are frequently so much alike as to be interchangeable. These findings remain generally important, even if some of Buschke's inferences are no longer compatible with the latest genetic concepts.

Maltarello (1957) took x-rays of the right hands and wrists of 98 twin pairs between 2 and 18 years of age (29 male and 29 female MZ, 12 male and 4 female DZ; 24 opposite-sex). Intra pair comparison revealed similarity in the ossification processes in 57 out of 58 MZ pairs, as compared to dissimilarity in 31 out of 40 DZ pairs. The process of ossification appeared to be slower in male subjects, with significant intra-pair differences in the opposite-sex pairs.

Kühne's twin studies of the spine put the final touch on his earlier genealogical investigations (10,000 roentgenograms on 121 individuals from 23 families). An appraisal of the twin data requires a brief review of his previous findings.

When anatomists talk of a normal spine and its well-defined characteristics, they are fully aware of a number of possible variations which may be found at certain locations. Predilection sites of this kind are (a) the junction of cervical and dorsal columns, where the seventh cervical vertebra may have a pair of more or less deformed ribs attached, or the first dorsal vertebra may have no corresponding ribs; (b) at the junction of dorsal and lumbar columns, ribs may be attached to the first lumbar vertebra, or the twelfth dorsal may have none; (c) the fifth lumbar vertebra may be fused with the sacrum (sacralization) or the first sacral vertebra may form a part of the lumbar column rather than the sacrum; (d) similar anomalies between sacrum and coccyx.

The tendency of these malformations to occur in an "ascending" or "descending" direction was shown by Kühne (1931) to be concentrated in families. Ascending variations of this kind include dorsalization of the seventh cervical vertebra, ankylosis of the ribs at the level of the twelfth dorsal vertebra, and sacralization of the fifth lumbar vertebra. Descending varieties are ankylosis of the ribs at the level of the first dorsal vertebra, dorsalization of the first lumbar vertebra, permanent detachment of the first sacral vertebra, and sacralization of the first coccygeal vertebra.

To explain the observed variations on a genetic basis, Kühne assumed a single factor type of inheritance, with dominance of the factor for the ascending variety and with recessiveness of that for the descending variety. Accordingly, individuals showing the ascending trait would be either homozygotes or heterozygotes, while only homozygotes would be able to manifest the descending trait.

In line with this working hypothesis, 58.5% of the spines classified in Kühne's series of cases (from Berlin) were ascending in type; 34.2% descending; and 7.3% intermediate. Dividing the intermediate group between the other two types, Kühne obtained a 6.4 ratio (63.1:36.9%) in twins as well as in single born individuals.

In Kühne's twin study (53 MZ, 35 same-sex and 50 opposite-sex DZ pairs), which was extended to the parents of the twins, x-rays of the spine showed a tendency to intra-pair similarity only in one-egg twins, with variations in penetrance and phenotypic expression of the genes concerned. For instance, in the spines of the two MZ pairs in Figure 122, one sees evidence of concordance for the descending trait in the first

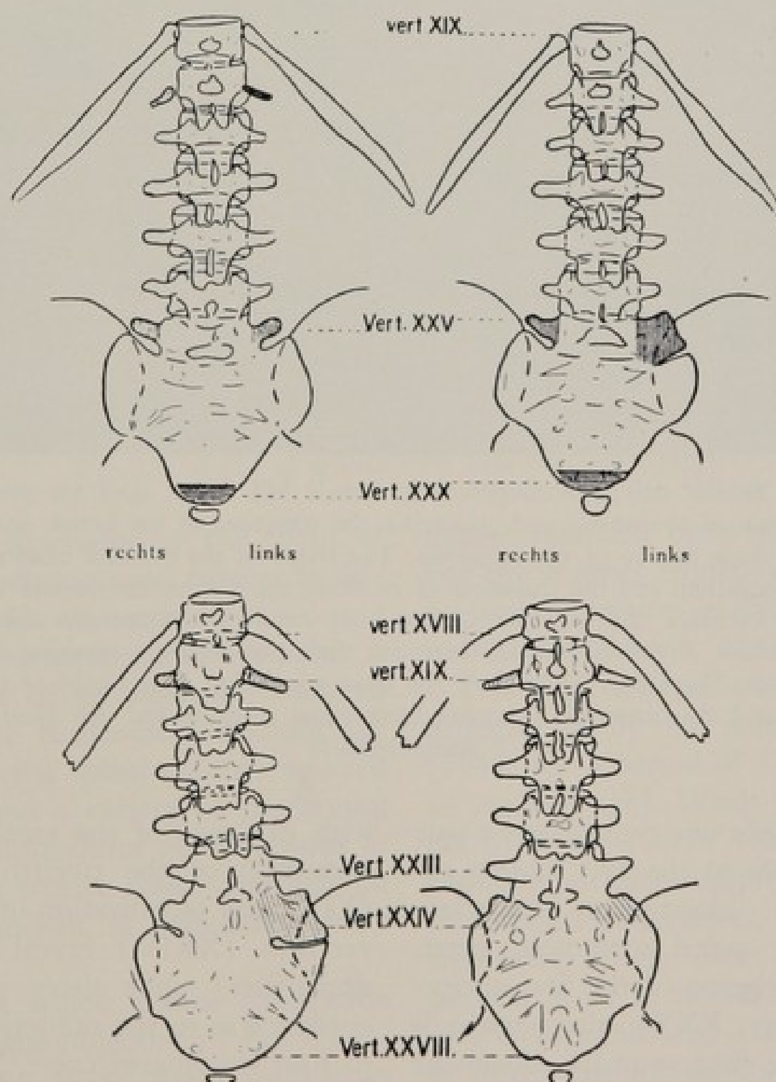
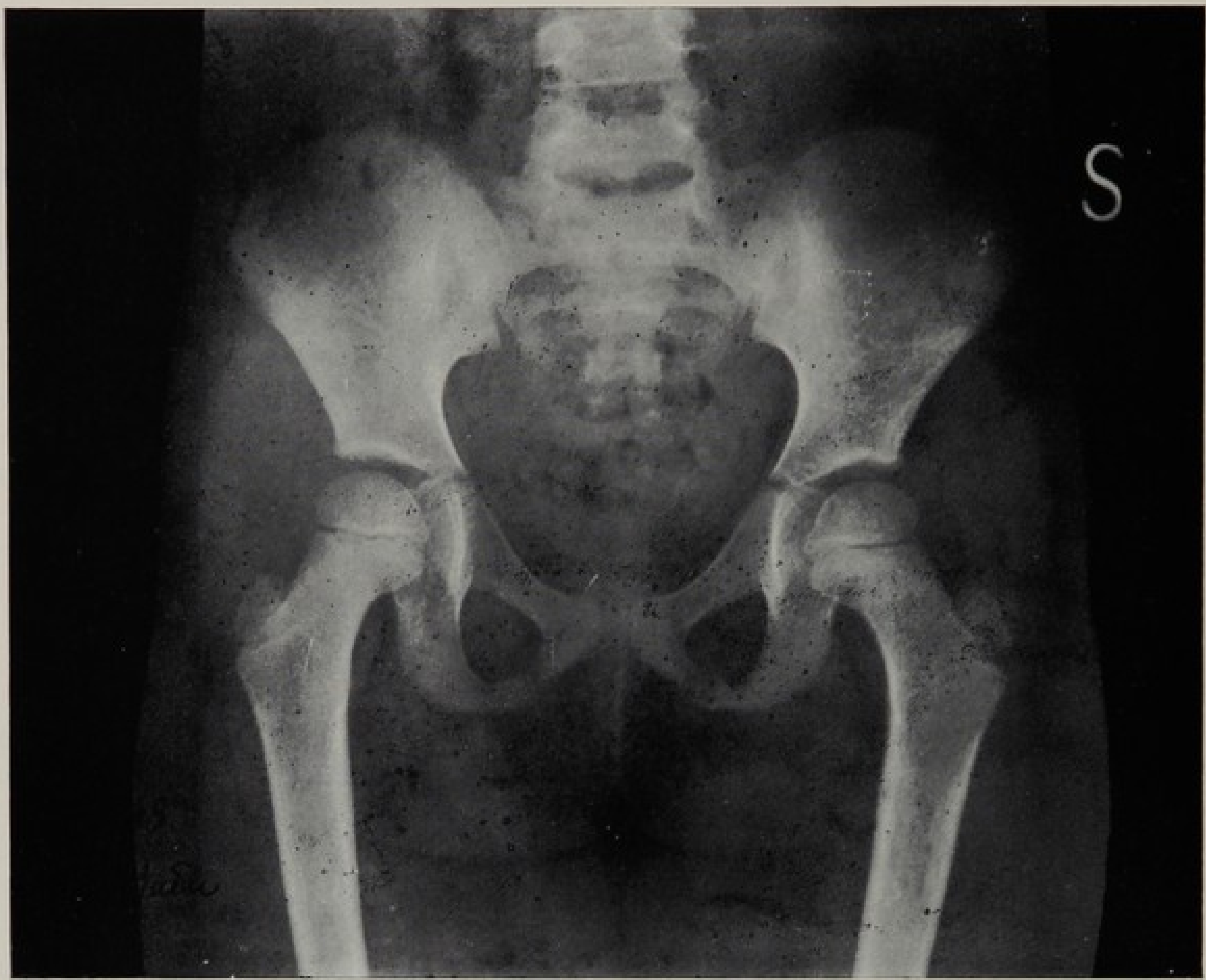


Fig. 122. Metameres of the lower vertebrae in two pairs of MZ twins (Kühne) (rechts=right; links=left).



Figs. 123 and 124. Similar pelvic development in female MZ twins, aged 6½ years, with identical degree of calcification of the nuclei and epiphyses, the structure of the bones, and the direction of the trabeculae and their degree of condensation. The shape of the femoral head and its angulation, the form of the acetabulum and the thickness of its floor, the height, course and undulations of the femoral epiphyseal cartilage and the surrounding bony condensation are also alike. The iliofemoral ligaments have identical direction and development, their prolongation reaching the same point on the head of the femur. The femur necks show the same angulation. The nuclei of calcification of the greater trochanter and the obturator foramina have equal margins and are identical in shape and size (Gedda).

pair. However, while one twin shows a pair of rudimentary ribs in the first lumbar region (vert. XX), incomplete lumbarization of the first sacral metamere (vert. XXV) and sacralization of the first coccygeal segment (vert. XXX), the cotwin is discordant for the first anomaly, dissimilar as to the type of the second anomaly, and concordant as to the third.

On the other hand, in the second pair with evidence of the ascending trait, lumbarization of the twelfth dorsal vertebra (XIX) and sacralization of the fifth lumbar vertebra (XXIV) reveal phenotypic dissimilarities, while there is complete concordance as to the reduction of the sacrum to four metameres (vert. XXVIII) and the fusion of the last sacral vertebra with the coccyx. According to Kühne, observations of this kind are explained by variations in

Fig. 124. X-ray of second twin (see previous figure).

penetrance and especially by the effect of such prenatal environmental factors as differences in position or nutrition.

Apparently, the structure of the spine is the end-product of an interplay between opposing genetic tendencies directing the development of the spinal column upward or downward and a variety of modifying factors either endogenous or exogenous in nature. In other words, these variations do not occur at random, as demonstrated by twin studies.

The order in which cranial ossification takes place was the objective of Pryor's investigations (1936, 1939). Apart from looking for another criterion for distinguishing one-egg and two-egg twins, the investigator reported intra-set similarity in the one-egg Kerner triplets and threefold ossification differences in the Schense quadruplets (two MZ boys, two DZ girls).

The same triplets were followed roentgenographically by Sontag and Reynolds (1944) for a period of 12 years (from 2 to 14 years of age). While differing in height, the three boys were concordant for a rare anomaly, an extra epiphysis at the base of the second metacarpus, and showed many similarities in the onset of the ossification process in all 26 nuclei investigated. There also were significant differences, particularly in the rate of ossification on various age levels. The most pronounced range of variability as to the time of ossification was observed in the metatarsal nuclei.

In view of these findings (chronological similarity in the development of many ossification nuclei, with possible differences in some nuclei), the investigators warned against basing a zygosity diagnosis on a single roentgenographic series. They concluded that certain environmental factors (acquired characteristics of a metabolic nature) are capable of modifying the genetic pattern of ossification.

Other interesting twin studies included those by Turpin (1938) on two sets of MZ twins (six-year-old girls concordant as to the bilateral absence of ossification nuclei in the lunate bone and two-year-old boys with similar findings in the hamate); by Turpin, Tisserand and Piton (1938) on a one-egg pair of six-year-old boys showing reversed asymmetry in a double ossification nucleus in the lunate; and by Turpin, Tisserand, Bernyer and Caspar-Fonmarty (1942) on intra-pair similarities in the configuration of the frontal sinuses. This third investigation (19 MZ and 17 DZ pairs) was extended to the form of the scapula and revealed a higher degree of intra-pair similarity in one-egg than in two-egg twins.

From our Rome material, similar pelvis x-rays of 6½-year-old female MZ twins are shown in Figures 123 and 124. Considering the age level of these girls, the observed intra-pair similarity is remarkable.

4. SKIN, HAIR, DERMATOGLYPHICS

Among genetically determined *skin* characteristics, pigmentation was studied by v. Verschuer (1939) in 135 MZ and 103 DZ pairs. In the former group complete intra-pair similarity was found in 117 pairs, and some dissimilarity in the others, apparently due to the effect of different environmental factors. In the two-egg group only 57 pairs showed intra-pair similarity.

According to Schiller (1936), dissimilarities are sometimes observed in one-egg pairs where one twin is forced by heart disease, infantile paralysis or a similar ailment to remain indoors and abstain from sports. As a rule, the unaffected twin is more tanned, especially on the extremities.

Freckles have been of interest to twin researchers since Siemens (1924) stressed their usefulness in making a zygosity diagnosis (intra-pair similarity in one-egg twins only). In Decking's series (1926), one-egg twins were alike as to the presence (42 pairs) or absence (22 pairs) of freckles, with freckled twins showing marked intra-pair similarity in the size and other details of the spots. Quantitative differences were found only in older pairs, probably due to outside influences. In the two-egg group, 11 pairs were classified as similar as to the presence or absence of freckles, and 19 pairs as dissimilar. Darker freckles were usually seen in the darker-skinned twin.

According to v. Verschuer's data (1933), 70 MZ pairs were similar as to freckles, with quantitative differences in 16 pairs. Of 66 DZ pairs, 10 were completely similar, 27 partly similar, and 29 dissimilar. In another series of one-egg twins, complete intra-pair similarity as to freckles was reported in 25 pairs, and almost complete similarity in 16 pairs.

Remarkable instances of intra-pair similarity as to freckles in one egg pairs were described by Waardenburg (Fig. 125), as well as by the author (Plates VII, VIII and IX). Schiller's data on freckles are summarized in Table XL.

Twin studies on lentigines were conducted by Siemens (1923) in a series of 45 MZ and 23 DZ pairs, by Scholl (1926) in 93 MZ and 76 DZ sets, and by Schokking (1931) in a series of five MZ and nine DZ pairs. All investigators reported a higher intra-pair similarity in one-egg than in two-egg twins.

According to Scholl, the correlation co-

Plate VII. Moles on the face of the mother of MZ twins pictured in Plates VIII and IX.

Fig. 125. Intra-pair similarity as to the distribution of freckles in MZ twins (Waardenburg).

Table XL

INTRA-PAIR SIMILARITY (IN PER CENT) IN HAIR COLOR AND SKIN PIGMENTATION (SCHILLER)

	MZ	DZ					
		Male		*Female*		*Opposite-Sex*	
		Similar	*Dissimilar*	*Similar*	*Dissimilar*	*Similar*	*Dissimilar*
Pigmentation of skin	100	50	50	47	53	77	23
Color of hair	100	23	77	24	76	45	55
Freckles	100	80	20	58	42	79	21

efficient computed for MZ pairs was .887 ± .03, and that for DZ pairs, .68 ± .06 (as against a coefficient of .12 ± .1 for two unrelated persons of the same age). By and large, these findings were confirmed by Weitz (1924), Paulsen (1925) and Meirowsky (1925), at least from a quantitative point of view (number of lentigines observed).

Regarding the genetic aspects of the *hair*, the main characteristics investigated by means of the twin study method have been the following: (a) color, (b) texture, and (c) hair follicles.

In his studies of hair color, Dahlberg found marked intra-pair similarity in one-egg twins. Also, he observed an interesting pair in which one member lost her hair following erysipelas. When the hair grew in again, it was darker than before and darker than her cotwin's but only for a while. A few years later, when the girls reached the age of 19, their hair color was once more identical, the cotwin's having gradually darkened, too.

This observation is in line with a phenomenon that leads to temporary intra-pair dissimilarity with respect to certain twin characteristics and may be referred to as "asynchronism." The temporary lack of synchronism in the development of a gene-specific trait in one-egg twins (acceleration or retardation) may be interpreted as a difference in the time of determination of the phenotype and may often be explained by the effect of environmental circumstances on only one member of a pair. In Dahlberg's case, discordance as to erysipelas apparently hastened the development of a genotypically determined chromatic variation.

Using Fischer-Saller's color scale in a series of 215 MZ and 156 DZ twins, v. Verschuer compared intra-pair variations in hair color, too (Table XLI). In another

Table XLI

HAIR COLOR VARIATIONS (v. VERSCHUER)

	MZ	*DZ*
Similar hair coloring	75.8%	7.0%
Slightly different hair coloring	13.5%	15.3%
Dissimilar hair coloring	10.7%	77.5%

sample (219 MZ and 148 DZ pairs), he observed intra-pair similarity as to hair texture in 100% of one-egg pairs and in 79% of two-egg pairs. The relatively small difference between the two groups was ascribed to the fact that straight hair was a common characteristic of the parent population.

In Brauns' study (1934), 43 MZ pairs were classified as similar, 5 MZ pairs as nearly similar, and 2 MZ pairs as dissimilar as to hair color, although all MZ twins showed intra-pair similarity as to hair texture (compared with 43 out of 54 DZ pairs). In the two-egg group, 13 pairs were similar, 14 nearly similar, and 27 dissimilar as to hair color. The technical difficulties encountered in studying the hair of young children were stressed by Brauns as well as by Schiller (1936) and Gesell and Thompson.

Variations in the distribution of lanugo and other types of hair (pubes, etc.) were studied by Weber (1939) in a large series of twins, and found to be so characteristic that they were recommended as a useful aid in zygosity diagnosis.

Kiil's hairline studies on Norwegian men (1948) revealed three forehead types in the general population, with frequencies of 44 : 28 : 28%, and complete intra-pair similarity as to these types in all 30 MZ pairs (with a tendency to reversed asymmetry) and in 43% of 28 DZ pairs. The detailed results of this investigation are summarized in Figure 126.

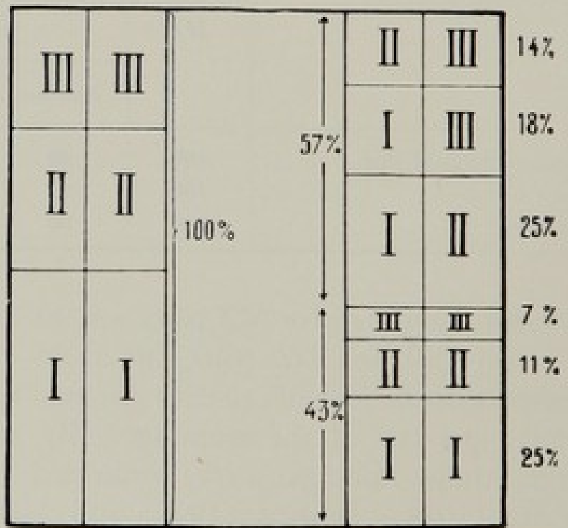


Fig. 126. Intra-pair similarity in three hairline types in MZ (left) and DZ (right) twins (Kiil).

Plates VIII and IX. MZ twins 9½ years of age who have inherited from their mother (Plate VII)
a less-marked but concordant development of facial moles (observed by Gedda).

Plate IX.

Wrinkles (permanent in old people) and temporary forehead lines (following stimulation) were analyzed by Bühler (1934) in 42 MZ and 43 DZ pairs. The intra-pair similarity observed in one-egg twins extended to the number, direction and spacing of wrinkles, but there were considerable variations in the branching. Other differences were ascribed to reversed asymmetry.

As to the extent and distribution of subcutaneous fat tissue, Weninger (1933) described lower abdomen dissimilarities in a one-egg pair (also studied by Routil). Other intra-pair differences were noted by Sieder in the ocular region, and by Ogawa (1940) in the volume of fetal fat tissue of of the cheek.

Of particular importance has been the study of *dermatoglyphics*, both in twin research and in identification procedures (dactyloscopy). While the Bertillon system was devised largely for the purpose of identifying criminals, Galton (1892) was the first to compare the fingerprints of the right hands (index, middle and fourth fingers) of same-sex twins. He noted marked similarity in some cases (as did Bertillon in an accidentally discovered pair referred to by Apert), and dissimilarity in others.

The theory that there are two different types of twins in man, one-egg and two-egg, was confirmed by Wilder (1904, 1908, 1919) on the basis of dermatoglyphic studies in 50 pairs of twins and 16 sets of triplets. Intra-pair similarity in identical twins was observed not so much in minute details as in the general trends of fingerprint patterns.

Poll (1914) and Ganther and Rominger (1923) were more guarded in their conclusions. The former fingerprinted 83 "probably" one-egg pairs, two sets of triplets and one pair of pygopagous twins; the latter fingerprinted five MZ and 42 DZ pairs classified according to the fetal-membrane method. Poll's study included no pair with similar dermatoglyphic patterns in all fingers, and only a few with similar patterns in nine fingers.

In the one-egg series analyzed by Ganther and Rominger, a higher degree of intra-pair similarity was found than ever occurred in two-egg twins, but the similarity extended only to seven or nine fingers. Since at least one finger always showed some disparity, the investigators erroneously regarded the fetal-membrane method as more useful for zygosity classification than a comparison of fingerprints.

Leven (1924) confirmed in 23 same-sex pairs that the intra-pair similarity in one-egg pairs (15 were diagnosed as such) consistently exceeded that in two-egg pairs (8), both qualitatively (type of pattern) and quantitatively (number of ridges). On the other hand, Lauterbach (1925), who studied 149 same-sex and 63 opposite-sex pairs, questioned the value of palm prints in identifying one egg twins.

In view of a greater intra-pair similarity in one-egg than in two-egg twins, Dahlberg (1926), Waardenburg (1926) and Korkhaus (1927) favored the use of fingerprints in zygosity diagnosis. A similar attitude was taken by Montgomery (1926) with respect to footprints (investigated in 57 same-sex and 30 opposite-sex pairs). In his opinion, definite intra-pair similarity is indicative of monozygosity, while its absence does not preclude it.

In Japan, detailed dermatoglyphic studies were conducted by Karugami (1926), Obonai (1926), Kishi (1927), and Komai (1928). Karugami reported complete correspondence in ridge counts in 2 of 15 same-sex pairs, and in none of 5 opposite-sex pairs. Kishi's conclusion was a lesser degree of intra-pair variability in same-sex (49 sets)

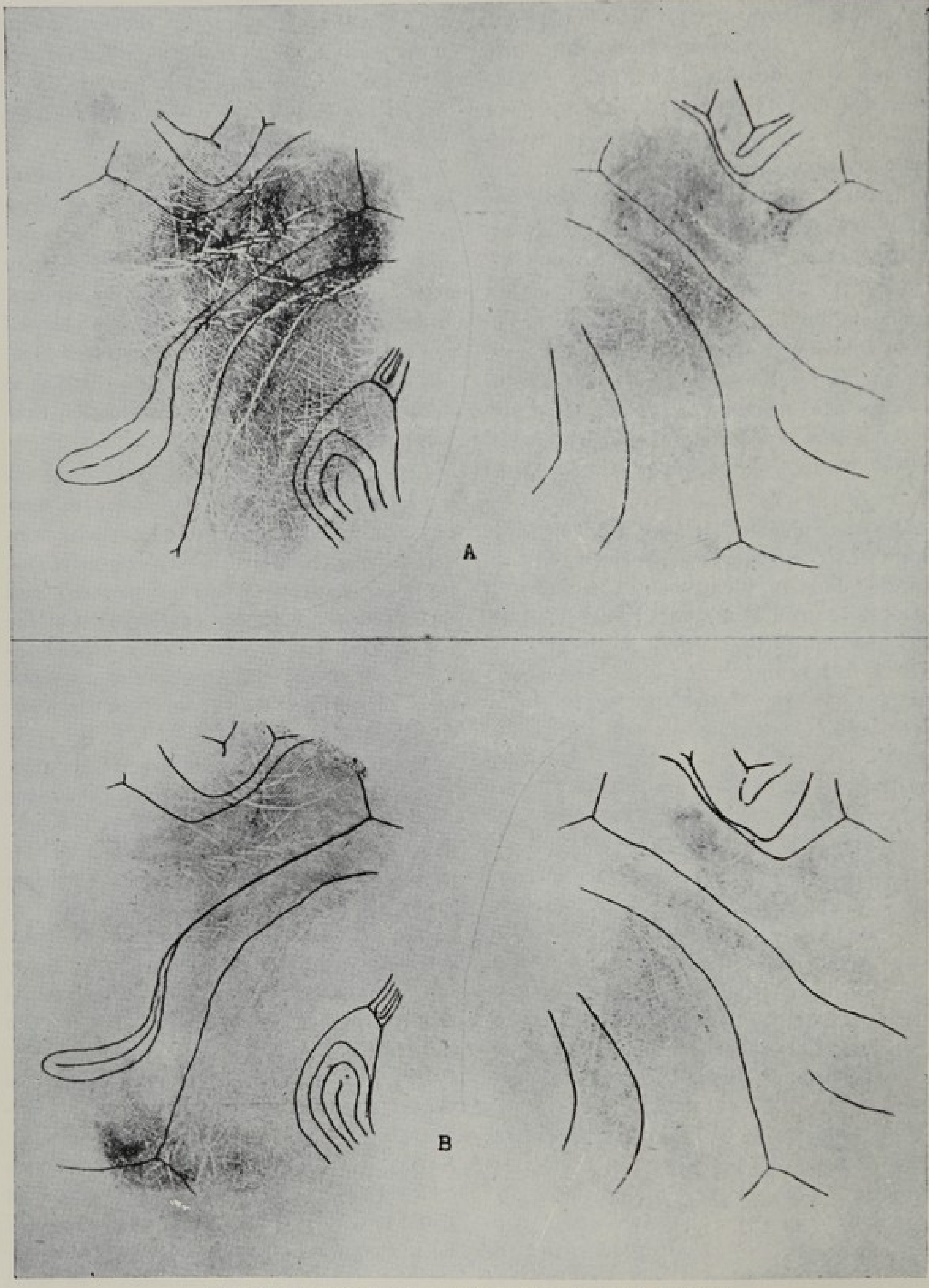


Fig. 127. One-egg similarities in fingerprints (Taku Komai).

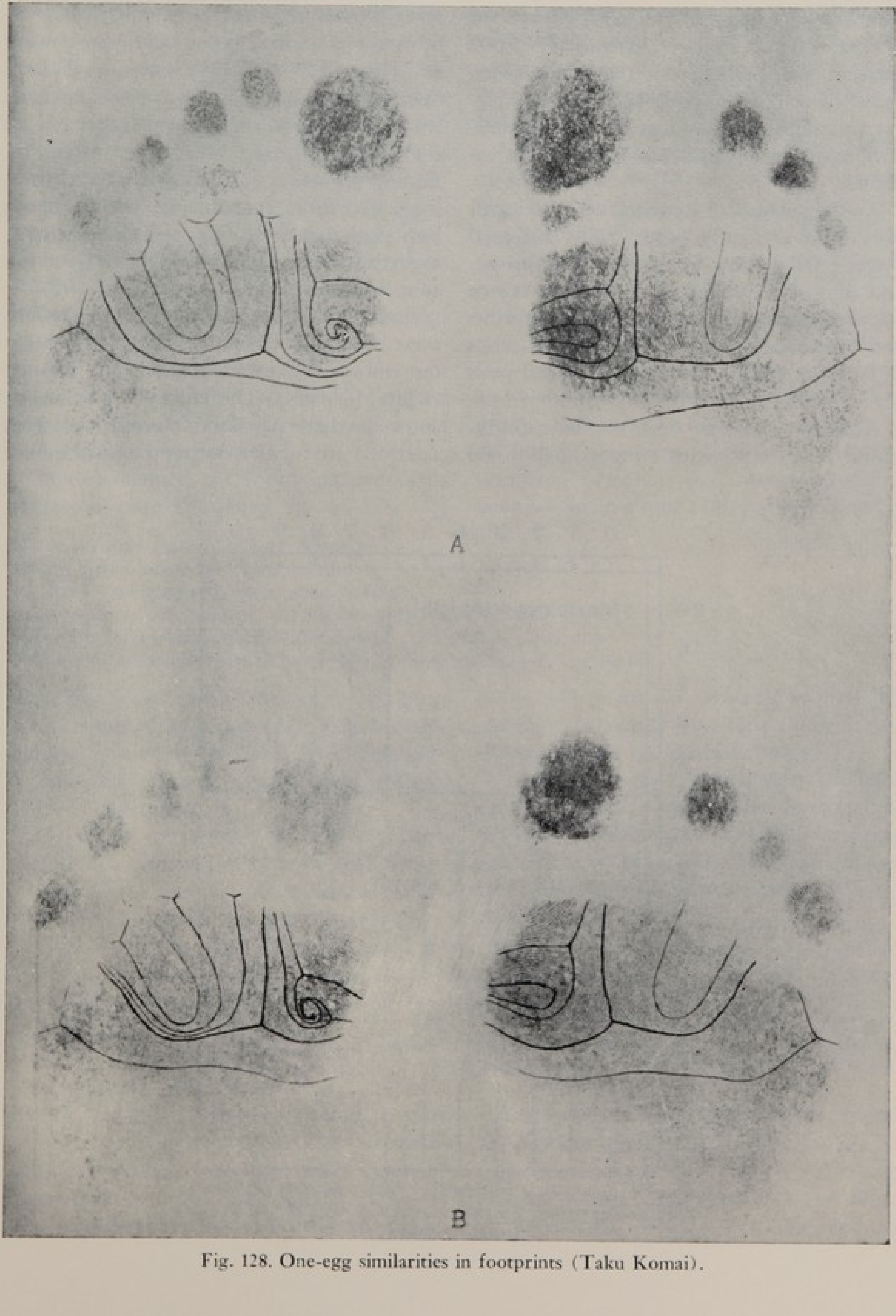


Fig. 128. One-egg similarities in footprints (Taku Komai).

than in opposite-sex (11 sets) twins. In Obonai's report on approximately 2,000 pairs, it was pointed out that some pairs, classified as monozygotic because of physical (including sex) and psychological similarities, differed considerably in their fingerprints.

Komai's material consisted of a series of nine same-sex pairs with fully analyzed finger-, palm- and footprints; 55 same-sex and nine opposite-sex pairs, as well as one set of triplets whose palm and fingerprints had been studied; and a fingerprinted series of 166 same-sex and 30 opposite-sex pairs placed at his disposal by Obonai.

According to these data, the dermatoglyphics of one-egg twins (fingers, palms and feet) proved to be far more alike than those of two-egg twins of the same or opposite sex (Figs. 127 and 128), with qualitative differences in not more than two fingers in the one-egg group and more frequently in the two-egg group. Another interesting finding in one-egg twins was that dermatoglyphic cross resemblance (between the two right hands or feet of twin partners) exceeded internal resemblance (between the two hands or feet of one twin).

Equally illuminating were the data obtained by Bonnevie (1923, 1924, 1927, 1931) on embryos, family trends, and one-egg twins (36 pairs). The embryological work showed that papillary corium patterns (dermis) are formed during the third month

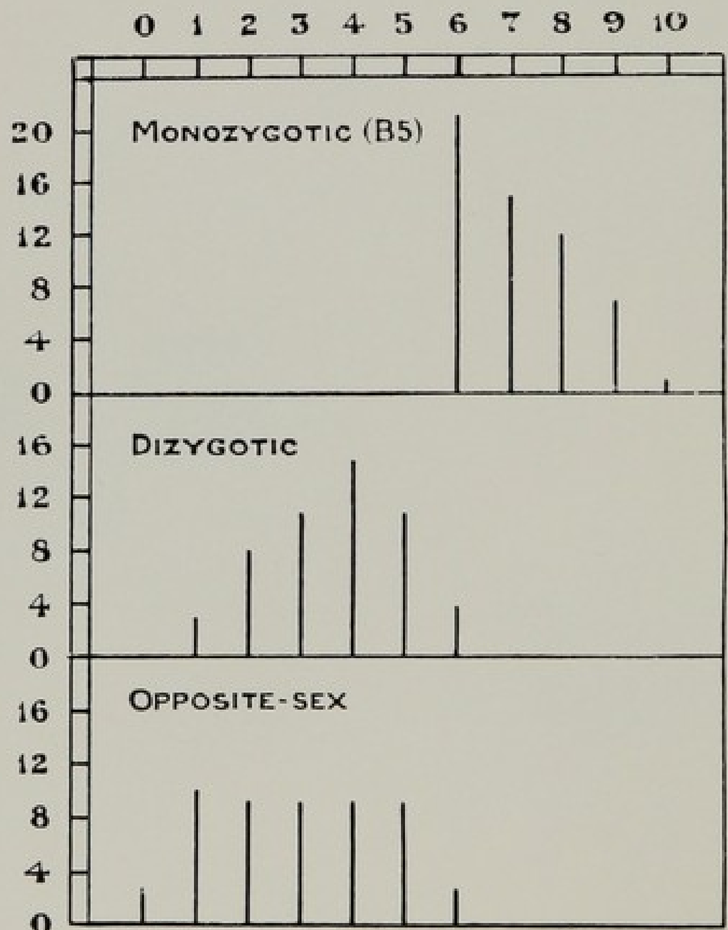


Fig. 129. Intergroup comparisons of the number of fingers with similar prints, with the number of pairs shown on the ordinate (Stocks).

of development, while their extension into the epidermis is completed by the end of the fourth month.

The genetic analysis of family data pointed to the operation of genes V and v as the determinants of quantitative variations in fingerprint patterns, with one gene producing thick skin and a relatively small number of ridges, and the other gene producing thin skin and a high value for ridges. Further quantitative variations were ascribed to localized epidermal thickenings (epidermal pads or *Epidermispolster*) controlled by another set of genes (R or U according to whether the pads were on the radial or ulnar side of the hand, and r and u when unexpressed).

In this manner, the following genotypic formulae were computed:

UV for a total number of 6-15 ridges
Uv for a total number of 16-21 ridges
vv for a total number of more than 21 ridges
vv or uu for a difference of 0-4 ridges on the radial or ulnar side
Rr or Uu for a difference of 5-10 ridges on the radial or ulnar side
RR or UU for a difference of more than 10 ridges on the radial or ulnar side

In Bonnevie's twin studies, 30 MZ pairs were classified as genotypically completely similar according to this dermatoglyphic system, four pairs as partly similar, and two pairs as dissimilar.

From the standpoint of zygosity diagnosis, the fingerprint studies of Stocks (1930, 1933) proved of particular value. While one-egg twins were found to have at least six fingers with similar dermatoglyphic patterns on both hands, two-egg twins had six or less (Fig. 129). The finding was explained on the basis of a strong familial tendency to the formation of similar dermatoglyphic patterns, with one-egg twins showing an even more pronounced degree of similarity because of their origin from one ovum.

In Newman's fingerprint analysis (1930) of 50 MZ and 50 DZ pairs, a more frequent intra-pair similarity was observed in one-egg than in two-egg twins (Fig. 130). Comparison of the corresponding prints for each finger yielded 347 points of intra-person similarity (right and left hands) and 351 points of intra-pair similarity (two right or left hands) in the one-egg group, and 36 and 248 points, respectively, in the two-egg group. Without the fingerprints of the little fingers (frequently similar even in two unrelated persons), the intergroup difference was even larger (288 points in one-egg twins, 168 points in two-egg twins). The observed intra-pair similarity in MZ pairs did not extend to "minute details."

Based on the number of ridges, the quantitative analysis yielded even more striking intergroup differences. Dividing his ridge counts into 17 categories, Newman obtained the following comparative results:

	MZ	DZ
Between r. and l. hands of the same subject	0.93±0.01	0.93±0.01
Between r. hand of the first & r. hand of the second twin	0.92±0.01	0.34±0.08
Between l. hand of the first & l. hand of the second twin	0.93±0.01	0.50±0.07
Between r. hand of the first & l. hand of the second twin	0.91±0.02	0.47±0.07
Between l. hand of the first & r. hand of the second twin	0.93±0.01	0.40±0.08
Between both hands of twin partners	0.95±0.01	0.46±0.08

According to Schreiber (1930), himself an identical twin, a study of his family (the parents and their five children, including a pair of twins) confirmed that the fingerprints of twin partners are "not identical"

Fig. 130. Similar left ring fingerprints of female MZ twins, with some minute differences (Newman).

but are anatomically more similar than those of other family members. Additional corroborative data were provided by Hara's (1932) study of 45 MZ and 48 DZ pairs of twins, by Sanders' (1932) report on two female sets of MZ triplets, and by the quantitative analyses of Geipel (205 MZ, 129 same-sex DZ, and 76 opposite-sex DZ pairs) and v. Verschuer (1934).

The fingerprints of two pygopagous pairs were studied by Cummins and Mairs (1934) and Cummins (1936). Those of the Gibb sisters (Fig. 72) were found to be more similar to the fingerprints of the father than of the mother. In addition, there were some interesting intra-pair differences which were ascribed to the given disturbance in embryonic development. In fact, the thumb print of one twin resembled that of a sister rather than of her cotwin.

Wendt (1955), applying a method called "Individuelle Musterwert," studied the intra-pair similarity of fingerprints in 100 MZ and 100 same-sex DZ twin pairs. None of the MZ pairs had dissimilarity values of more than 5 (19 pairs showed no dissimilarity and 51 less than two dissimilarities) while DZ pairs showed complete similarity in only five cases, the others being distributed over various degrees of dissimilarity (33 dissimilarities in one case!).

Palm prints of 200 same-sex (100 one-egg, 100 two-egg) and 50 opposite-sex pairs were investigated by Meyer-Heydenhagen (1934). In MZ twins, intra-pair similarities were found to be sufficiently consistent to form a reliable basis for zygosity classification in 90% of the cases. Homolateral similarity was observed only in certain asymmetrical features and did not exceed the degrees of internal resemblance with respect to other characteristics.

In a set of Canadian MZ quadruplets, both palm- and foot-prints were reported by MacArthur and MacArthur (1937) to be entirely dissimilar.

"Almost complete" intra-pair similarity in the dermatoglyphics of MZ twins was

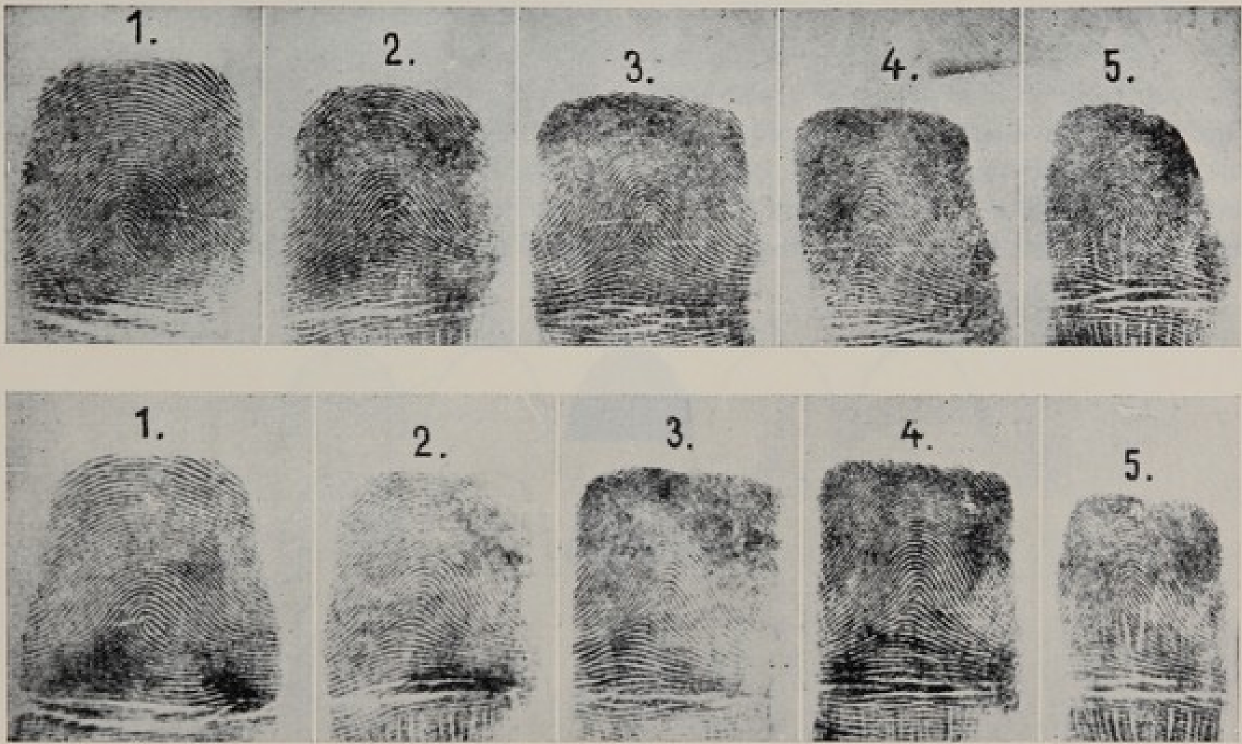


Fig. 131. Right hand fingerprints of MZ twins.

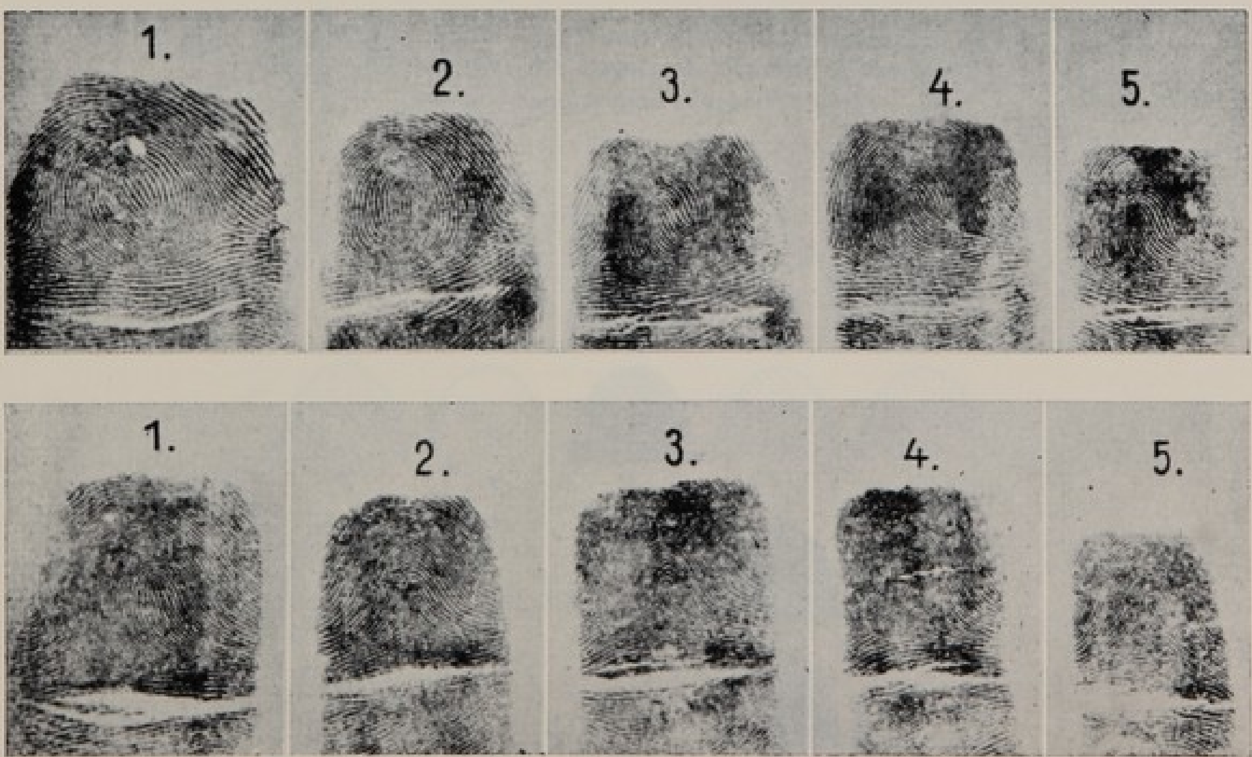


Fig. 132. Right hand fingerprints of DZ twins.

described by Lotze (1937), as against the usual dissimilarity observed in DZ pairs (Figs. 131 and 132). A major difference was seen only in the prints of the fourth fingers. The investigator concluded that a correct zygosity diagnosis could be made dermatoglyphically "in a large number of cases." He added, however, that some doubtful cases remain in which monozygosity may be decided only after considering other characters.

Using Geipel's method, although with some misgivings, Ennenbach (1939) studied intra-pair differences in fingertip pad structure (*Polsterbild*) in a series of 25 MZ and 25 DZ pairs (Figs. 133 and 134). Classifica-

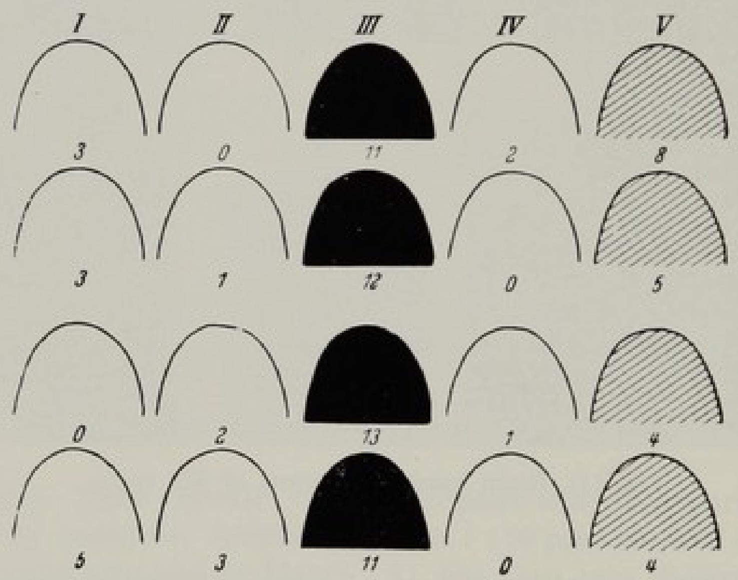


Fig. 133. Fingertip pad structure (*Polsterbild*) in MZ twins (Ennenbach): Strongly developed (black); medially developed (shaded); undeveloped (white).

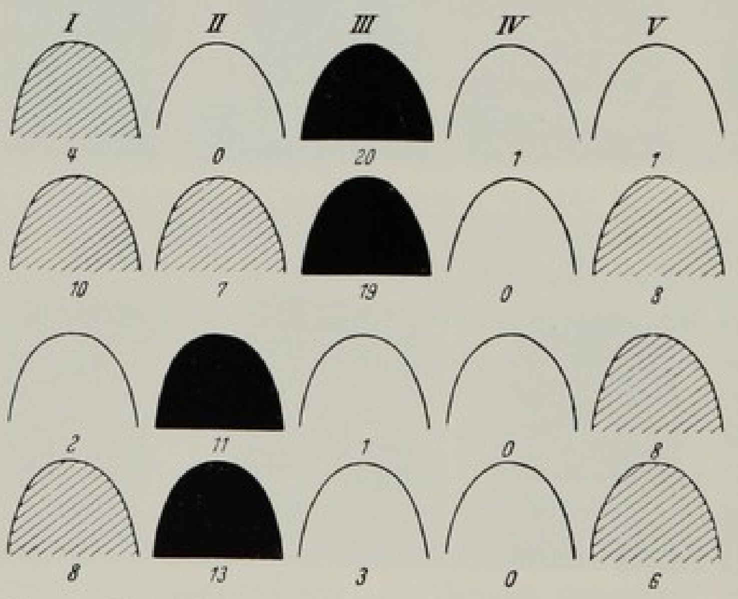


Fig. 134. Fingertip pad structure in DZ twins (Ennenbach).

tion of the pad structures as strongly developed, medially developed or underdeveloped revealed that 24 MZ pairs and only 14 DZ pairs fell into the same category, with average intra-pair differences of 4.0 and 11.5, respectively, for the one-egg and two-egg groups. A difference of 15 or more on this scale was considered indicative of dizygosity. In fact, 22 DZ pairs and only two MZ pairs proved to be dissimilar according to this quantifying system, thus confirming the value of dermatoglyphics within the scheme of the modern similarity method.

Further corroborative evidence was provided by Schiller (1942) who analyzed the

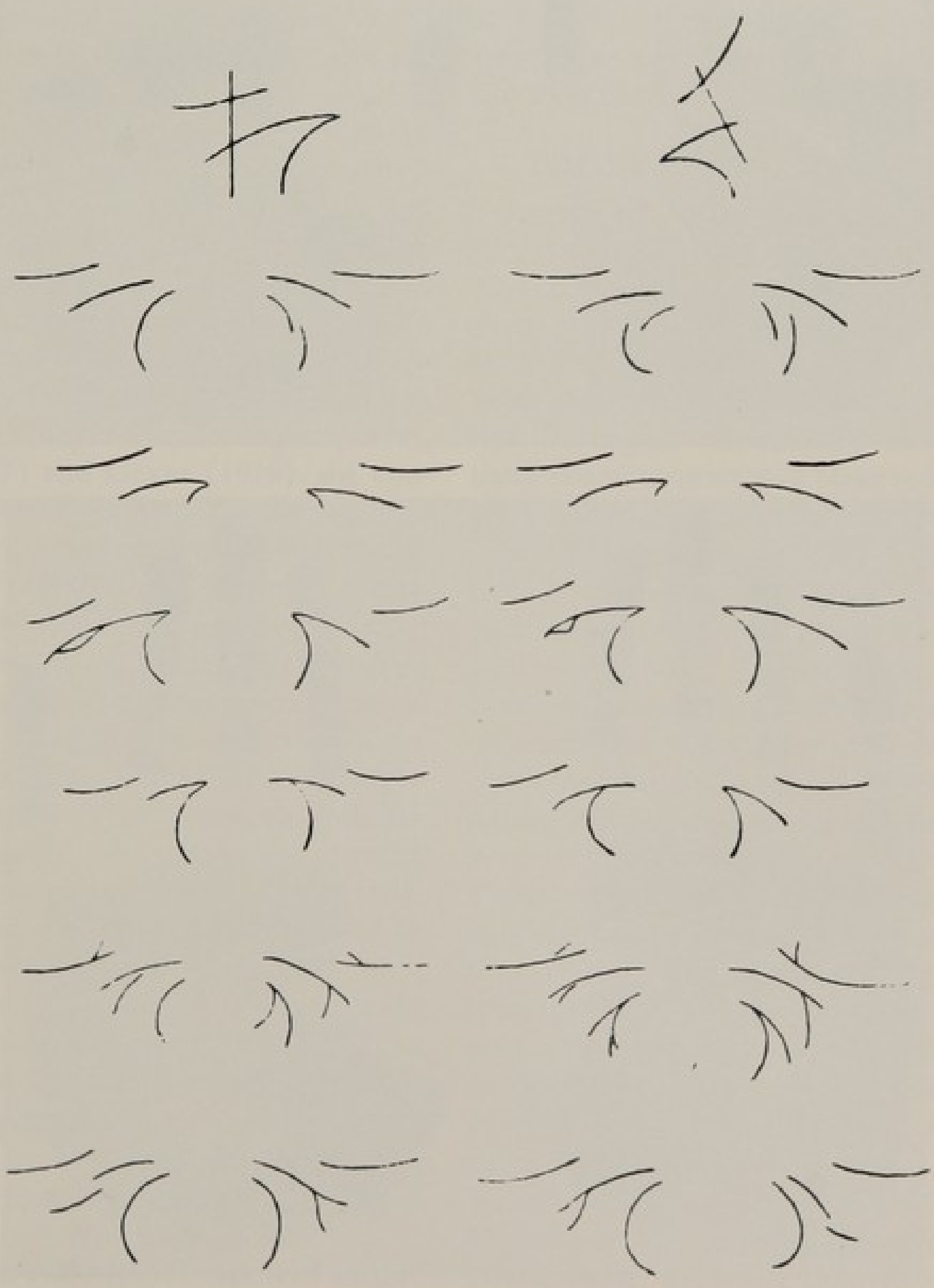


Fig. 135. Palmar creases in MZ pairs showing various combinations of homolateral, bilateral and mirror-image similarity (Schiller).

Figs. 136 and 137. Palmar creases in female MZ twins (Schiller), with normal configuration in one twin (upper figure) and with simian crease in the other (lower figure), particularly well developed on the left hand.

palm prints of 128 MZ and 189 DZ pairs. Complete intra-pair similarity, with precise correspondence in direction, depth and length of palmar creases, was observed in 74.4% of MZ pairs and in none of the DZ pairs. There were various combinations of homolateral, bilateral and mirror-image similarity as schematically shown in Figure 135. While 6.4% of MZ pairs and 28.4% of DZ pairs were classified as partly similar, 19.2% of MZ pairs and 71.8% of DZ pairs appeared to be entirely dissimilar.

Schiller also studied the frequency of the simian crease (Figs. 136 and 137), which is a horizontal line dividing the upper and middle thirds of the palm, particularly in cases of mongolism and other pathological conditions. Adding her own observations (4 pairs) to those of Perlstein (1927), Grünberg (1928), Bettmann (1932), Weninger (1930, 1933), Meyer-Heydenhagen (1934), Portius (1937) and Geyer (1939), she concluded that 12 of the 18 MZ pairs reported in the literature had shown intra-pair similarity as to possession of a simian crease.

Tillner (1954) studied the frequency of the simian crease (and its transitional forms) and its similarity in a large population including 375 MZ, 360 same-sex and 226 opposite-sex DZ pairs, as well as 2045 singleborn individuals. The similarity and dissimilarity figures for the three zygosity groups of twins clearly indicated the hereditary nature of the simian crease and of its transitional forms.

It may also be mentioned in this connection that thorough dermatoglyphic analyses were made by Ford, Brown and McCreary (1941) in a pair of MZ twins with pyloric stenosis, and by Ford and Frumkin (1942) in a one-egg pair concordant as to mongolism.

Osato and Awano (1957) reported a study by Saito (1950), on the degree of similarity of finger and palm ridges in a material composed of 138 twin pairs (65 MZ, 48 same-sex DZ, 25 opposite-sex DZ). Both finger and palm ridges revealed a higher degree of intra-pair similarity in the MZ than in the DZ group (75.4% of MZ pairs showed similarity in at least eight fingers, as compared to 45.7% of same-sex DZ pairs and 36.0% of opposite-sex DZ pairs). Examining MZ twins belonging to different age groups it was found that similarity as to finger ridges was higher between 6 and 8 years of age than in later age groups.

5. THE EYE AND ORBITAL REGION

Among twin studies dealing with the eye, v. Verschuer's (1927) report on 60 MZ and 45 DZ pairs included data on such variations in *eyebrows* as length, relative position, height and shape of the arch, interbrow distance, configuration, color and the like. Intra-pair dissimilarity in regard to these characteristics was observed in 22 DZ pairs and in only one monozygotic set.

In Waardenburg's (1930) series of 137 MZ and 55 same-sex DZ pairs, detailed ocular measurements were taken in a group of 23 one-egg pairs. Marked intra-pair similarity was established with respect to concurrent eyebrows, the direction of the principal meridians, the distance between the medial canthus and the lower lacrimal orifice, and every disorder of refraction, of the cornea as well as total refraction, thus confirming the genetic theory of refractive disturbances of the eye. In addition, measurements of the distance between pupils revealed no intra-pair difference in nine pairs; a difference of less than 0.5 mm. in eight pairs; of 0.5-1.0 mm. in four pairs; and 1.5-3.0 mm. in two pairs.

According to v. Rötth's (1937) data on 43 MZ, 49 DZ and 5 unclassified sets of young twins, intra-pair similarity was generally pronounced in the one-egg group with respect to eyebrows, periocular skin

Figs. 138 and 139. Similar ocular characteristics in MZ twins, shown with eyes open (upper figure) and partly closed (lower figure).

Figs. 140 and 141. Dissimilar ocular characteristics in DZ twins (Sieder), with eyes open (upper figure) and partly closed (lower figure).

pigmentation, corneal diameter and color of the iris, with corresponding similarities between two-egg partners tending to be less than one half. Another concomitant of monozygosity was a trend toward reversed asymmetry in certain eyebrow characteristics.

Equally detailed observations regarding eyebrows, eyelids and eyelashes (Figs. 138-142) were made by Sieder (1938) in a series of 20 MZ and 20 DZ pairs. Some comparative results of this investigation are

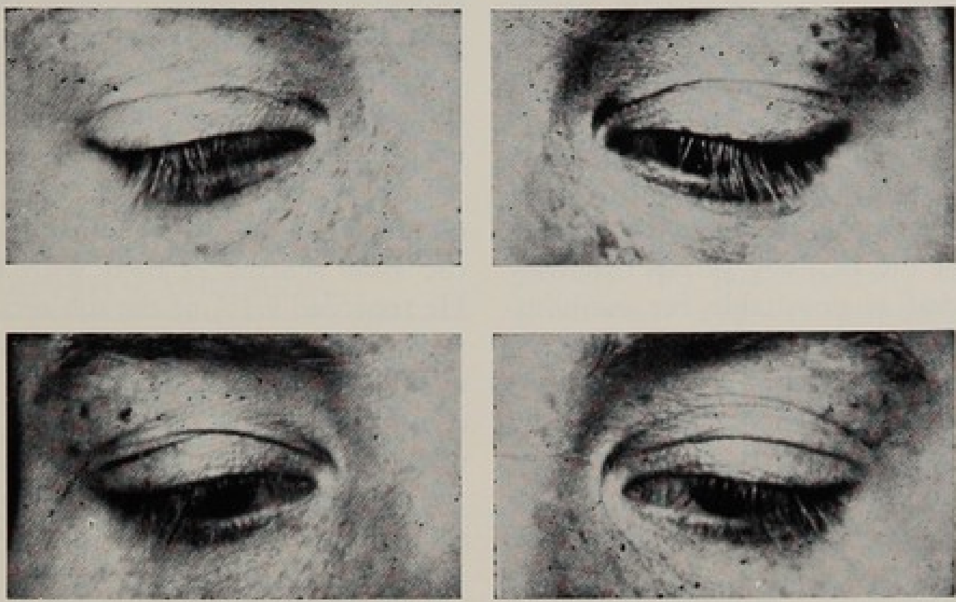


Fig. 142. Concordance as to epicanthus in MZ twins (Sieder).

Table XLII

OCULAR VARIATIONS IN 20 MZ AND 20 DZ PAIRS (SIEDER)

Characteristic	*Number of Dissimilar Pairs*	
	MZ	*DZ*
General appearance	1	8
Fat pads	4	10
Form of eyebrows	3	8
Position of eyelid fold	0	5
Form of eyelid fold	0	6
Form of medial canthus	0	3
Total height of upper eyelid	2	7
Height of orbital section	1	3
Height of tarsal section	2	4
Demarcation of superior orbital sulcus	1	1
Demarcation of orbito-palpebral sulcus	0	3
Thickness of covering fold	2	7
Size of covering fold	2	7
Form of lateral canthus	1	2
Tarsal sulcus	1	6
Form of lower eyelid	3	8

presented in Table XLII. In addition, Sieder obtained the following mean intra-pair differences (in mm.) with Martin's method:

	MZ	*DZ*
Distance between lateral canthi	1.2	2.5
Distance between medial canthi	.6	2.0
Distance between pupils	.8	1.9
Height of upper eyelid	1.1	1.5

Sieder's conclusions were formulated as follows:

1. Except for the formation of fat pads, the structure of the soft parts of the eye is largely determined by genetic factors.

2. Since the soft parts of the eye do not develop as independent structures, they are subject to variations in phenotypic expression.

3. Although one-egg twins show a high degree of intra-pair similarity as to the morphology of the soft parts of the eye, a zygosity diagnosis cannot be based on these characteristics alone.

Janke's (1940) study of 72 MZ and 71 DZ pairs (plus one unclassified set) was largely concerned with problems of zygosity diagnosis. As to the characteristics of the eyebrows, complete intra-pair similarity was observed in 98.59% of one-egg pairs and 10.29% of two-egg pairs; incomplete similarity in 1.41 and 19.12% respectively; and marked dissimilarity only in the two-egg group (70.59%). The corresponding percentages for intra-pair similarity in eyelids varied from 71.79 in MZ twins to 10.0 in DZ twins, while the relative degrees of similarity as to eyelashes were so high even in the two-egg group that they were regarded as unsuitable for establishing a zygosity classification.

The importance of the *color of the iris* as a classificatory criterion was stressed by Siemens as well as by Dahlberg. The latter described a one-egg pair that was heterochromatic at birth (blonde with blue eyes, brunette with brown eyes) but equally brown-eyed at the age of 15 years. The temporary difference in the pigmentation of the iris was ascribed to extrinsic influences in the prenatal period.

In a series of 292 DZ twins, Dahlberg classified the color of the iris according to the same scheme as used with hair color. He recorded 9.2% of the subjects as brown, 82.9% as light and 8.9% as intermediate, establishing by calculations the independent determination of eye color in genetically dissimiliar twins.

Color and structure of the iris were also studied by Freerksen (1938) in 9 MZ and

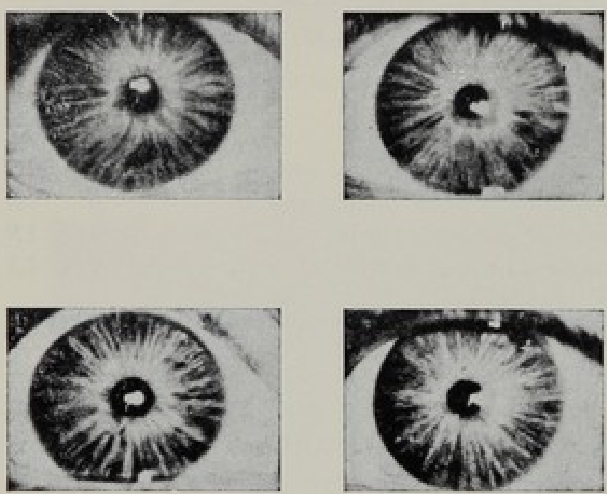


Fig. 143. Similar iris in female MZ twins.

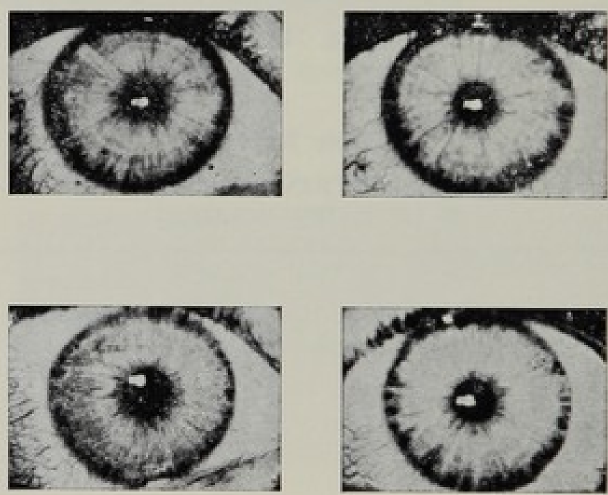


Fig. 144. Similar iris in female MZ twins.

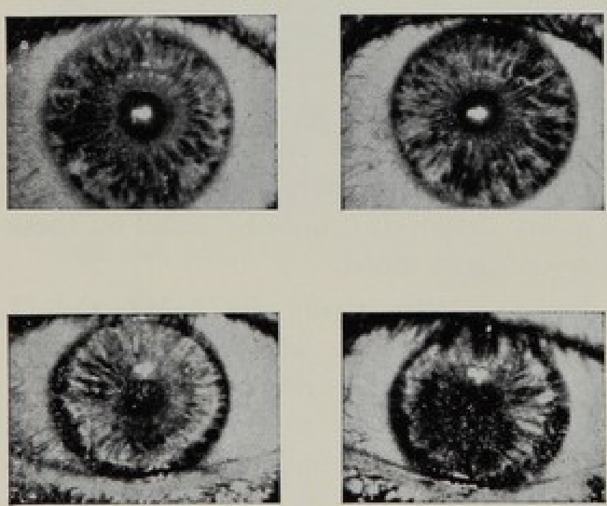


Fig. 145. Dissimilar iris in male DZ twins.

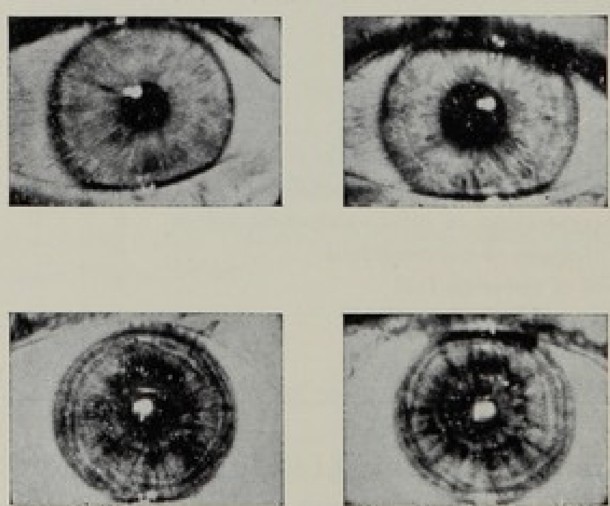


Fig. 146. Dissimilar iris in male DZ twins.

12 DZ pairs, by v. Verschuer (1933) in 256 MZ and 194 DZ pairs classified according to the color tables of Martin and Martin-Schultz (Table XLIII), and by Schwaegerle (1938) in 21 MZ and 19 DZ pairs (Figs. 143-146). Freerksen reported consistent intra-pair similarity in iris structure (although not in all minor details) in one-egg twins, and Schwaegerle was able to make a correct zygosity diagnosis in 36 pairs, using various aspects of the iris structure as the only criteria.

Table XLIII

INTRA-PAIR VARIATIONS IN THE COLOR OF THE IRIS (v. VERSCHUER)

	MZ	*DZ*
Color of iris similar	86.7%	13%
Color of iris slightly dissimilar	12.9%	15%
Color of iris dissimilar	0.4%	72%

Martin's color table was employed by Stocks (1933), too, to measure intra-pair differences in iris color. A difference of four or more points was found only in two-egg twins.

6. THE EAR AND THE NOSE

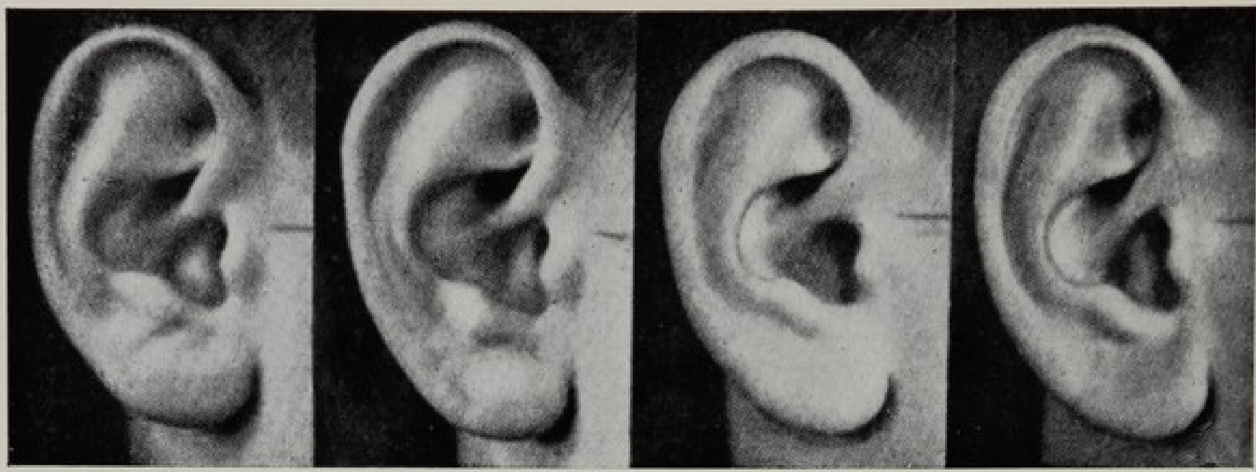
In the opinion of Dalla Volta and Chiarugi, the characteristics of the *outer ear* are less variable than fingerprints and therefore more suitable for zygosity classification. Using four different measurements in a series of 19 sets of twins, Dalla Volta (1924) demonstrated that intra-pair similarity and dissimilarity as to the given ear lobe features correspond with the zygosity type of twins.

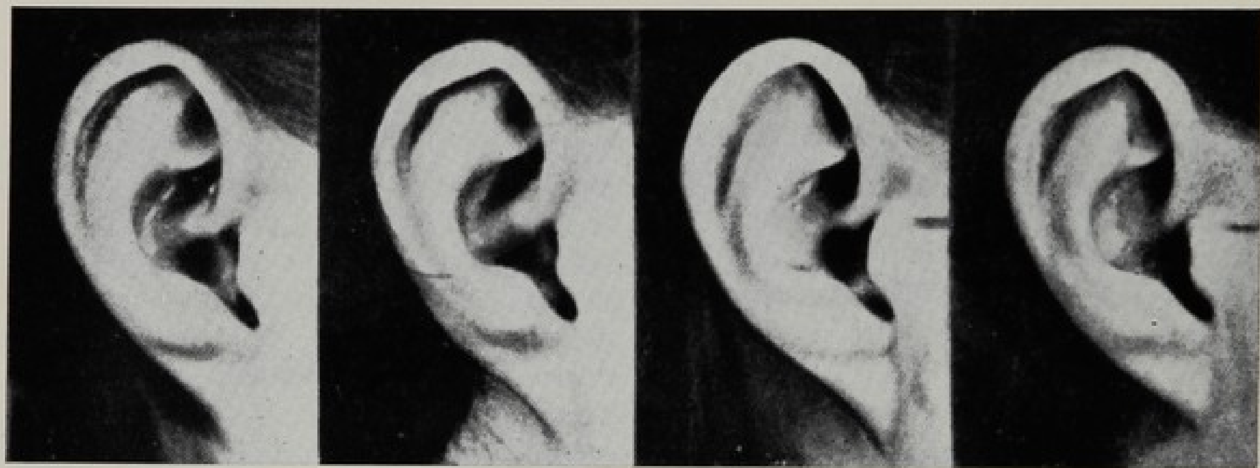
Dahlberg's (1926) study of outer ear characteristics, carried out with the aid of photographs, was extended to both intra-person and intra-pair comparisons (MZ and DZ twins as well as 100 unrelated persons paired off according to various kinds of similarity). While unrelated and two-egg pairs showed many differences, one-egg twins were distinguished by marked intra-pair similarity, thus precluding a significant effect of nongenetic factors on the structurization of the outer ear. Dahlberg emphasized this fact especially for purposes of an early zygosity diagnosis, since the facial features of twin infants are rarely sufficiently well defined to serve as a useful criterion.

In Quelprud's (1932) genetic analysis of human ear variations (180 pairs of twins), 19 measurements of the outer ear revealed a total mean intra-person and intra-pair difference of 1.2 mm. in the one-egg group, and a corresponding difference of 1.7 mm. in the two-egg group. Of 96 MZ pairs, 74 were similar as to the shape of the ears, while 20 were slightly dissimilar, and two definitely dissimilar. The corresponding distribution in the two-egg group was 1, 14 and 65 pairs.

Compared to the helix and Darwin's tubercle, the antihelix and its upper branchings were found to be least easily affected by external influences. The sulcus between helix and antihelix as well as the tragus and antitragus appeared to be structurally quite stable, with the shape of the *incisura intertragica* depending on the development of tragus and antitragus (Figs. 147-150). The prominence of the pinna was also shown to be a genetically determined character.

Darwin's tubercle was studied by both Meirowsky (1926) and Quelprud (1934). In the latter's investigation of male and female students, Hessian families and twin subjects from Berlin (116 MZ, 89 same-sex DZ and 38 opposite-sex pairs), the variability of the character proved to depend on age as well as sex. While the size of the tubercle increased with advancing age in the male, the opposite was observed in the





Figs. 147 and 148. Similar ear lobes in two pairs of MZ twins, for easier comparison shown in a side-by-side-position, with the left ears reversed and a short horizontal line drawn from the lower margin of the orbit to the upper margin of the external auditory meatus.

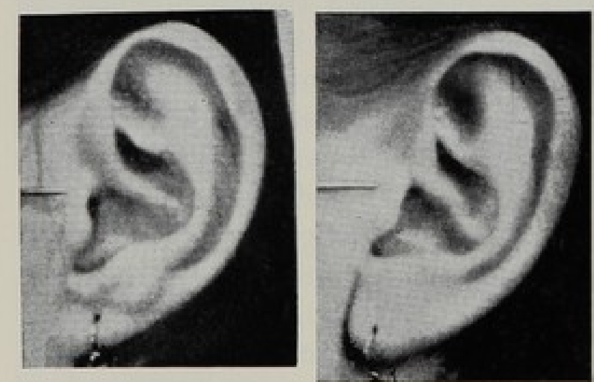


Fig. 149. Dissimilar ear lobe configuration in DZ twins.

Fig. 150. Similar prominence of pinnae in MZ twins (Quelprud).

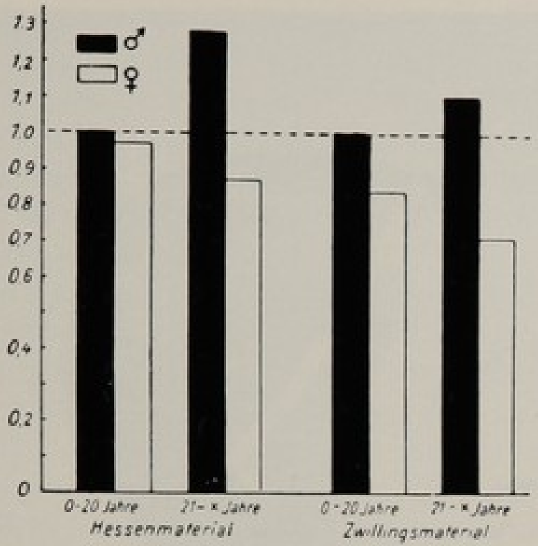


Fig. 151. Development of Darwin's tubercle before and after age 20, in Hessian population and twins (Quelprud) (Jahre = years; Zwillingsmaterial = turn material).

female (Fig. 151). On the other hand, the averages of the absolute values for twins of either sex were higher than those for the Hessian population, indicating the effect of some special factor operating in the prenatal development of twins.

Quelprud's data on the size and intra-pair distribution of Darwin's tubercle are summarized in Tables XLIV and XLV.

Table XLIV

MEAN INTRA-PAIR DIFFERENCES IN THE SIZE OF DARWIN'S TUBERCLE (QUELPRUD)

	MZ Pairs	*Same-Sex DZ Pairs*	*Opposite-Sex DZ Pairs*
Between homolateral ears	0.81	1.10	1.32
Between contralateral ears	0.88	1.14	1.29

Twin studies of the *nose* were reported by Leicher (39 MZ and 27 DZ pairs) and v. Verschuer (191 MZ and 129 DZ pairs). In Leicher's sample, complete intra-pair similarity was found in 31 MZ and 12 DZ pairs as regards such essential features as the length, breadth, position, shape and point of the nose, the form and appearance of the nostrils, and the shape and configuration of the septum. Slight differences were seen in eight MZ pairs, and distinct differences in 15 DZ pairs.

Table XLV

PRESENCE OR ABSENCE OF DARWIN'S TUBERCLE (QUELPRUD)

First Twin		*Second Twin*		*MZ*	*DZ of Same Sex*	*DZ of Opposite Sex*
R	L	*R*	*L*			
+	+	+	+	19	10	3
−	−	−	−	32	16	8
+	+	−	−	5	17	10
+	−	+	−	5	1	2
−	+	−	+	2	3	1
+	−	−	+	4	2	1
+	−	+	+	18	9	5
+	+	−	+	10	8	3
+	−	−	−	13	11	2
−	−	−	+	8	12	3
Total number				116	89	38

According to v. Verschuer's analysis, no intra-pair differences in nasal characteristics were detectable in 162 MZ pairs, minor differences in 29 MZ pairs, and gross differences in 86 DZ pairs. The observed variations in one-egg twins were ascribed to prenatal changes in cranial development, but were generally so inconsiderable that they did not seem to detract from the high diagnostic value of nasal characteristics, which were assumed to depend on the effect of at least five genetic factors.

The fact that the noses of one-egg twins may remain similar in shape, despite certain differences in profile and cranial diameters, was reported by Siemens (1927) who described the adolescent pair shown in Figure 152.

7. ORAL CAVITY AND TEETH

The outlines of the *lips* were studied by v. Verschuer (1933) in 190 MZ pairs. There

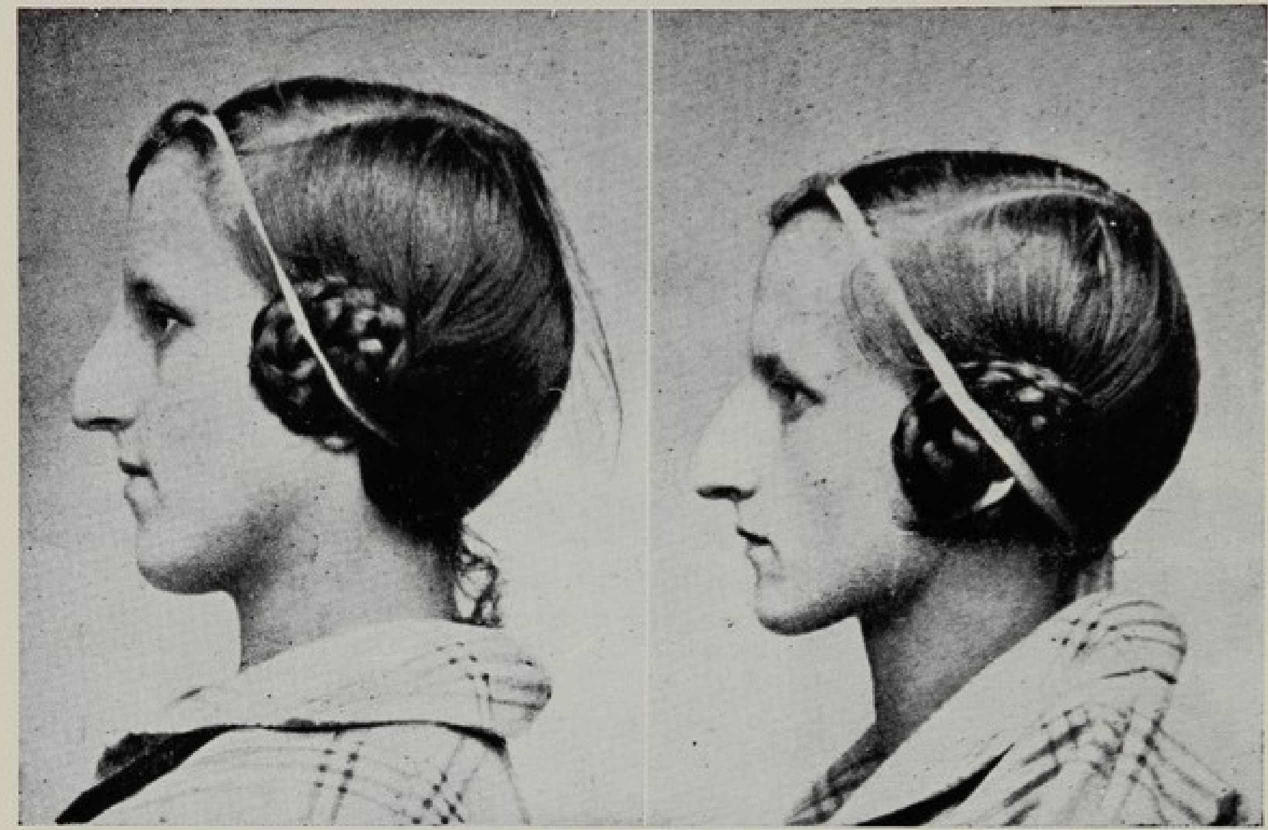


Fig. 152. Similar shape of nose in female MZ twins, aged 16 (Siemens).

were no significant differences in 162 pairs, and minor differences in 28 pairs.

The characteristics of the *tongue* were found to be so stable that Siemens included them in his scheme for determining zygosity. In v. Verschuer's series of 186 MZ pairs, no intra-pair differences were observed in 155 pairs, slight differences in 21 pairs, and considerable differences in 10 pairs. The corresponding distribution in the two-egg group was 57, 18 and 50 pairs.

Hypertrophy of the *papillae* of the tongue was described as a discordant condition in one DZ pair and two MZ pairs by Siemens and Hunold (1924) and in five DZ pairs by Kösters (1927). On the other hand, the latter investigator reported concordance in three MZ and three DZ sets. Additional papillary studies were carried out in Japan by Kikuchi (1935) in a series of 10 MZ pairs that showed marked intra-pair similarities, and by Ogawa (1940) in fetuses in connection with investigations of the parotid glands.

As to the structure of the *tonsils*, both palatal and pharyngeal, Curtius, Korkhaus and Thielmann (1930) reported greater intra-pair similarity in one-egg than in two-egg twins (Table XLVI). A certain inconsistency in the data on pharyngeal tonsils in the two-egg group was ascribed to the quantitative limitations of the sample.

Table XLVI
TWIN DATA ON TONSILS (CURTIUS, KORKHAUS AND THIELMANN)

Degree of Similarity	*Palatal Tonsils*		*Pharyngeal Tonsils*	
	MZ	*DZ*	*MZ*	*DZ*
Similar	30	7	24	7
Moderately dissimilar	4	4	2	—
Very dissimilar	4	14	1	—
Total	38	25	27	7

Twin studies of the oral cavity were often combined with data on the *jaws*, *fauces* and *teeth*. As early as 1846, Hider described two twin sisters with equally rose-colored teeth, attributed by Korkhaus to a transparent pulp due to a disturbance in dentin development.

In a series of four MZ and three DZ pairs, Bergfors (1923) found only minor intra-pair differences in the shape and arrangement of the teeth in the one-egg group, and more significant differences in the two-egg group.

More extensive studies were carried out by Siemens and Hunold (1924) in 56 MZ and 35 DZ twins of school age. The dental anomalies investigated were divided into the following categories: changes in form or size, structural anomalies, quantitative or positional changes, and malformations. The distribution of concordance and discordance was reported as follows:

	Concordant	*Discordant*
Gigantism of a canine	1 MZ pair	
Carabelli's tubercle	1 MZ pair	
	1 DZ pair	
Hyperplasia of dental tubercle	1 MZ pair	
Hypoplasia of enamel	7 MZ pairs	1 MZ pair
	2 MZ pairs (partly)	
	6 DZ pairs	6 DZ pairs
	2 DZ pairs (partly)	
Symmetrical agenesis of upper lateral incisor	1 MZ pair	
Symmetrically malturned teeth	27 MZ pairs	11 MZ pairs
	4 DZ pairs	18 DZ pairs
Asymmetrically malturned teeth	9 MZ pairs	19 MZ pairs
	6 DZ pairs	16 DZ pairs
Diastema of upper jaw	13 MZ pairs	13 MZ pairs
	8 DZ pairs	12 DZ pairs
Malformed palatine foramina	1 MZ pair	

In the opinion of the investigators, symmetrically malturned teeth are largely determined by genetic factors, while asymmetrical varieties are not.

Additional dental twin data of Siemens' school were published by Praeger (26 MZ pairs), Riepenhausen (36 MZ and 52 DZ pairs) and Kösters (33 MZ and 73 DZ pairs) in 1924, 1925 and 1927, respectively. Praeger's series included one MZ pair concordant as to supernumerary teeth, as well as some other one-egg pairs with concordance for dental hypoplasia and a congenital lack of an upper bicuspid. According to Siemens (1928), these observations indicated a genetic basis for Carabelli's tubercle, a symmetrical agenesis of teeth and the familial type of diastema, and a nongenetic etiology for hypoplasia of enamel and such positional defects as dislocation of teeth or a vertical-axis-malturning.

Unusual degrees of intra-set similarity as to various forms of orthodontic irregularities (occlusion, malturning of two upper right teeth in the same direction, etc.) were seen by Schroeter (1927) in a set of triplets, by Korkhaus (1942) in five sets of triplets and two sets of quadruplets, and by Steiner (1927) in two pairs of one-egg twins.

Other orthodontic twin data were contributed by Bachrach and Young (1927) from a series of 107 MZ, 70 same-sex DZ and 62 opposite-sex pairs (with discordance rates of 26.2± 2.9% in the one-egg group and 51.5±3.0% in the two-egg group, and with similar positional irregularities in one-egg twins either on the same or opposite side); by Stanton (1928) with interesting observations on a pair of one-egg twins (labial malposition of upper lateral incisors) and by Goldberg (1929, 1930) with comparative findings on a series of 15 MZ pairs in the age group 3½ to 24 years (greater homolateral intra-pair differences in dental arches than contralateral intra-person differences) and on another series of 50 MZ pairs (reversed asymmetry as to a congenital lack of upper lateral incisors in two pairs, as to malturned medial incisors, and other anomalies).

Korkhaus' twin studies (1929, 1930, 1931) extended to variations in deciduous and permanent dentition, the structure of teeth (formation of crown and roots), malformations of jawbones, and the like. With respect to the structure of the masticatory surface of the crowns, the investigator observed "a surprising degree of intra-pair similarity in one-egg twins," especially in the molars and bicuspids and on the palatal side of the incisors. The similarities made "one twin almost an exact copy of the other" and included the direction of pattern lines and their finest branches, the height and deviation of ridges, the formation of minute protuberances and the extent of dentinal hyperplasias. By comparison, the degree of intra-pair similarity in two-egg twins was far more limited.

Twin data on two unusual formations, the dental tubercle and Carabelli's tubercle, were analyzed by Korkhaus (1930), v. Verschuer (1933) and Zeiger (1934). Intra-pair similarity in one-egg twins was reported by Zeiger (14 pairs) and Korkhaus (42 pairs) as to the dental tubercle, and by v. Verschuer (69 out of 70 pairs) as to Carabelli's tubercle. In the two-egg group, 4 pairs were similar, 6 pairs dissimilar and 2 pairs undetermined as to the dental tubercle, and 30 pairs were similar, 52 pairs dissimilar, and 16 pairs undetermined as to Carabelli's tubercle.

The average intra-pair percentage difference in the width of upper medial incisors was computed by Korkhaus as .16±.02 in 22 MZ pairs, and as 2.13±.35 in 19 DZ pairs. Corroborative evidence for the genetic determination of the width of incisors was provided by Wolf's (1938) data, although his estimate of the average intra-pair percentage difference in one-egg twins was somewhat larger (.41±.07) than that of Korkhaus. As to the total size of the teeth, especially that of the crowns, Korkhaus doubted the significance of environmentally conditioned variations, except for lateral incisors and wisdom teeth.

On the assumption that the structure of teeth could be appraised by their color, Korkhaus (1930) used a color wheel to obtain twin data (with Curtius) on dental coloration. The observed intra-pair similarity in one-egg twins far exceeded that in two-egg twins (Table XLVII). Those minor variations seen in three MZ pairs occurred in elderly persons and were ascribed to prolonged external influences which may slowly modify the genetically determined basic color.

Table XLVII

INTRA-PAIR VARIATIONS IN THE COLOR OF TEETH (KORKHAUS)

	No. of Pairs	*Similarity*	*Slight Differences*	*Strong Dissimilarity*
MZ	51	48	3	—
DZ	33	11	6	16
DZ	9	2	2	5

In view of Wheeler's theory of a connection between color of teeth and pigmentation in other parts of the body, Korkhaus studied the correlation between dental coloration and the color of hair and eyes. However, Pearson's correlation coefficients relating eye, tooth and hair colors were found to be small and statistically not significant. It was concluded, therefore, that the assumed relationship was spurious.

While discordance as to supernumerary teeth was observed by Korkhaus in one DZ pair, concordance with respect to the agenesis of certain teeth was described by him in one DZ and two MZ pairs. In one of the latter pairs, one twin lacked the lateral incisors, and the other the second bicuspid. In another series of 14 MZ and 11 DZ pairs, concordance as to roentgenographically verified agenesis of incisors and bicuspids was reported by Korkhaus and Zeiger in all MZ and 4 DZ pairs.

Intra-pair similarity as to certain forms of malturning in one-egg twins was explained by Korkhaus as the result of "a primary torsion of the dental germ plasm." Concordance as to symmetrically malturned teeth was recorded in 117 out of a total of 192 MZ pairs (Siemens and Hunold, Korkhaus), and as to asymmetrically malturned teeth in 100 out of a total of 245 MZ pairs. Virtually no case of concordance with respect to pathological forms of malturning was seen in the two-egg group.

True forms of dental diastema were also regarded as genetically determined. In Korkhaus' series of 102 MZ and 47 DZ pairs, concordance was found in 12 one-egg and 2 two-egg pairs, and discordance in 1 one-egg and 7 two-egg pairs.

Further dental twin data were presented by Ritter (1933, 1937), Bratengeier (1934), Araki (1935), Euler and Ritter (1940), Noack (1941) and Haar (1942).

Ritter reported discordance as to supernumerary teeth in one MZ and two DZ pairs, and as to agenesis of teeth in six MZ pairs (explained by variations in penetrance of a very unstable genetic factor that may cause a "microscopic" form of the anomaly) and in nine DZ pairs (with "incomplete discordance" in two pairs). In another series of 96 MZ and 122 DZ pairs, Ritter observed concordance as to opistognathism in 2 MZ pairs (with discordance in 4 DZ pairs); as to prognathism in 1 DZ and 7 MZ pairs (with discordance in 12 DZ pairs); and as to superior deviation of incisors in 4 MZ pairs.

Bratengeier measured the width, length and thickness of teeth in 20 MZ and 18 DZ pairs, finding higher degrees of intra-pair similarity in the one-egg group. His data on the width of teeth are shown in Table XLVIII.

In a one-egg Japanese pair aged 28, Araki described concordance as to a supernumerary cone-shaped tooth embedded in the palate at the level of the right medial incisor.

While Noack's series of 3 MZ and 7 DZ pairs was too small to yield statistically significant intergroup differences with respect to the roof of the palate, the dimensions of dental arches and different types of bite, a large series studied by Euler and Ritter showed complete intra-pair similarity as to Carabelli's tubercle in all MZ and 10 DZ pairs, incomplete dissimilarity in 4 DZ pairs, and complete dissimilarity in 8 DZ pairs.

Haar's analysis of the width of incisors in 13 MZ and 14 DZ pairs revealed evidence of a gene-specific basis with marked modifiability by external factors, especially in the female. The same investigator described concordance for dental calculi and hypoplasia of the upper lateral incisor as well as simultaneousness in the eruption of teeth in one-egg twins. The observed mean intra-

Table XLVIII

MEAN INTRA-PAIR VARIATIONS IN THE WIDTH OF SOME TEETH (BRATENGEIER)

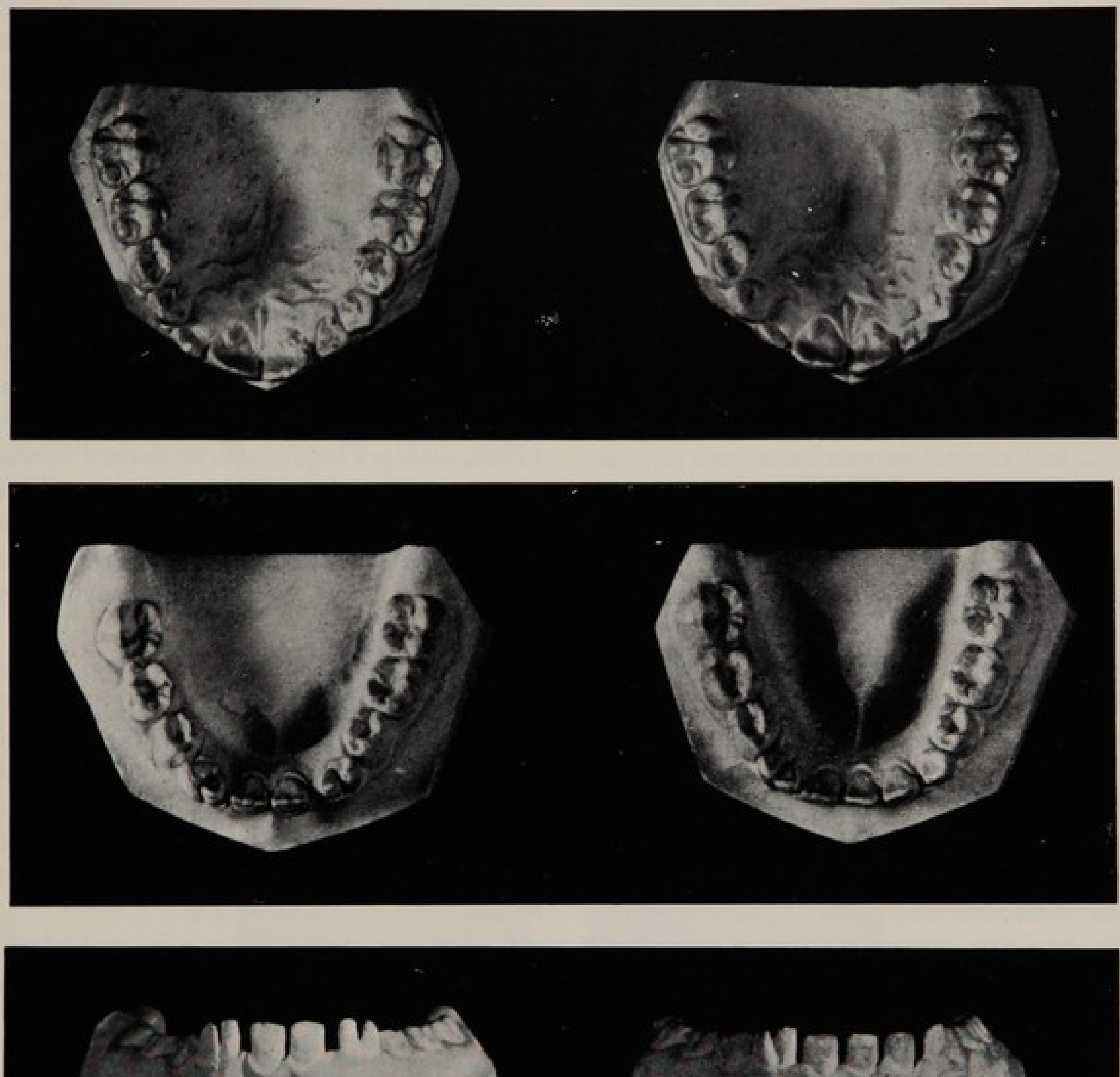
		Medial Incisor		*Lateral Incisor*		*Canine*	
		No.	*Normal Limits*	*No.*	*Normal Limits*	*No.*	*Normal Limits*
				Upper jaw			
MZ	L	20	1.88±0.30	19	4.24±0.68	8	3.16±0.80
	R	20	2.04±0.32	20	4.54±0.72	8	0.82±0.20
DZ	L	18	6.32±1.06	18	8.22±1.38	7	7.82±2.10
	R	18	5.34±0.90	18	6.16±1.02	8	5.08±1.28
				Lower jaw			
MZ	L	20	2.14±0.34	20	1.02±0.16	11	5.92±1.26
	R	20	2.54±0.40	20	1.06±0.16	11	3.72±0.80
DZ	L	17	6.46±1.10	18	6.30±1.06	12	6.92±1.42
	R	18	5.32±0.88	18	5.52±0.92	12	4.38±0.90

pair difference in unerupted teeth was .15 in MZ and .32 in DZ pairs.

This writer described similar varieties of diastema (probably falling within the limits of normal variability) in one-egg twins (Fig. 153), while Nico (1950) noted intra-pair similarity as to the structure of Carabelli's tubercle and the fusion of some teeth in another MZ pair (Figs. 154-156).

One of the most thorough studies was that of Lundström (1948) on dental size and occlusion in a Swedish sample of 100

Fig. 153. Similar varieties of diastema in seven-year-old MZ twins (Gedda).



Figs. 154-156. Dental arches of nine-year-old female MZ twins, with similarly constructed Carabelli's tubercles in the second deciduous and first permanent molars on both sides, and with fused lateral incisors and canines on both sides in one twin, and one side only in the second twin (Nico).

MZ and 102 same-sex DZ pairs ranging in age from 8 to 40 years. For the analysis of occlusion data, only children in the age group 12-15 were considered. The representativeness of the sample was open to some doubt.

The types of variation evaluated were the following: (1) between right and left sides of one individual; (2) between one-egg twins; (3) between two-egg twins. In etiological terms, the following modes of variability were distinguished; (1) contralateral intra-person variations due to extrinsic, intrinsic or genetic influences (asymmetrical variability according to Dahlberg); (2) environmental modifications; (3) genetically controlled variations (asymmetrical and environmental). The characteristics investigated included single-tooth characters, total width, spacing and position, width and length of dental arches, inclination of upper medial incisors on the bite, height of palatal roof from the bite plate, mesiodistal bite, and sagittal or vertical forms of overbite.

As to the width of upper medial incisors, the following mean differences were computed: intra-person, .19 mm.; intra-pair in MZ group, .22 mm.; intra-pair in DZ group, .52 mm.; asymmetrical variability, .12 mm.; environmental variability, .12 mm.; and genetic variability, .34 mm. The corresponding figures for upper lateral incisors were .37, .38, .58, .25, .05 and .35 mm., and those for canines were .18, .21, .39, .12, .06 and .25 mm. For all teeth, the range of intra-pair variations was from .32 to .34 mm. in the two-egg group, and from .14 to .34 mm. in the one-egg group. The range of nongenetic variations was given as .08 to .18 mm., and that of genetic variations as .2 to .38 mm.

Lundström concluded, therefore, that genetic factors play a significant part in the causation of these dental characteristics and are at least as important as environmental influences. This conclusion was reached although the sample apparently included a number of clearly pathological types of malocclusion.

8. CARDIOVASCULAR SYSTEM

Prenatal cardiological twin data, dealing with the size, weight and veins of the heart, the distribution and branchings of the coronary arteries, and the shape of the foramen ovale, were presented by Tsuchizya (1938, 1939). Despite the numerical limitations of the series of twin fetuses studied (10 MZ, 4 DZ and 3 unclassified pairs), the Japanese investigator reported greater intra-pair similarities in one-egg than in two-egg twins.

Roentgenographic heart studies in the postnatal period were carried out by v. Verschuer and Zipperlen (1929) as well as by Curtius and Korkhaus (1930). The results of the latter study (35 MZ and 22 DZ pairs), showing a high degree of intra-pair similarity in the one-egg group, are summarized in Table XLIX.

Gurevich's (1936) series consisted of 107 MZ and 86 DZ pairs ranging in age from 4 to 11 years. According to his data, variations in the size of the heart as measured diametrally appeared to be chiefly related to such "extrinsic" factors as height, weight, and circumference of the chest. In the opin-

Table XLIX

TWIN DATA ON THE SHAPE OF THE HEART (CURTIUS AND KORKHAUS)

	MZ		*DZ*	
	Number of Pairs	*Per Cent*	*Number of Pairs*	*Per Cent*
Very similar	24	68.5	4	18.0
Moderately similar	6	17.0	15	68.0
Dissimilar	5	14.5	3	14.0
Total	35	—	22	—

ion of Weitz, however, there is a pronounced similarity between the hearts of one-egg twins, with a difference often of less than one millimeter in horizontal diameters. Even such an unusual condition as a drop-shaped heart has been reported by v. Verschuer and Zipperlen (1929) to occur in both members of a one-egg pair (Fig. 157).

Gedda, Bresadola and Volta (1957) studied 11 MZ and 16 DZ pairs by means of both standard chest x-rays and transverse laminagrams. Their findings indicated a greater similarity of the cardio-vascular shadows among MZ twins. The authors thought that this might be ascribed to a lower incidence of functional variants in transverse laminagrams.

Ito (1948), as reported by Osato and Awano (1957) studied the environmental variability of the heart and the first section of the aorta in 139 twin pairs (30 male and 34 female MZ, 27 male and 22 female DZ, 26 opposite-sex pairs). The form of the heart was *very similar* in 59.3% of MZ and 8% of DZ pairs, *similar* in 32.8% of MZ and 40.8% of DZ pairs, and *dissimilar* in 7.2% of MZ and 42.8% of DZ pairs. The form of the first section of the aorta revealed practically the same degree of similarity. The shapes revealed a higher genetic conditioning than the measurements.

While intra-pair variations in the veins and peripheral nerves of the arm were studied by Kadanoff (1939), the anterior facial and frontal veins were the subject of

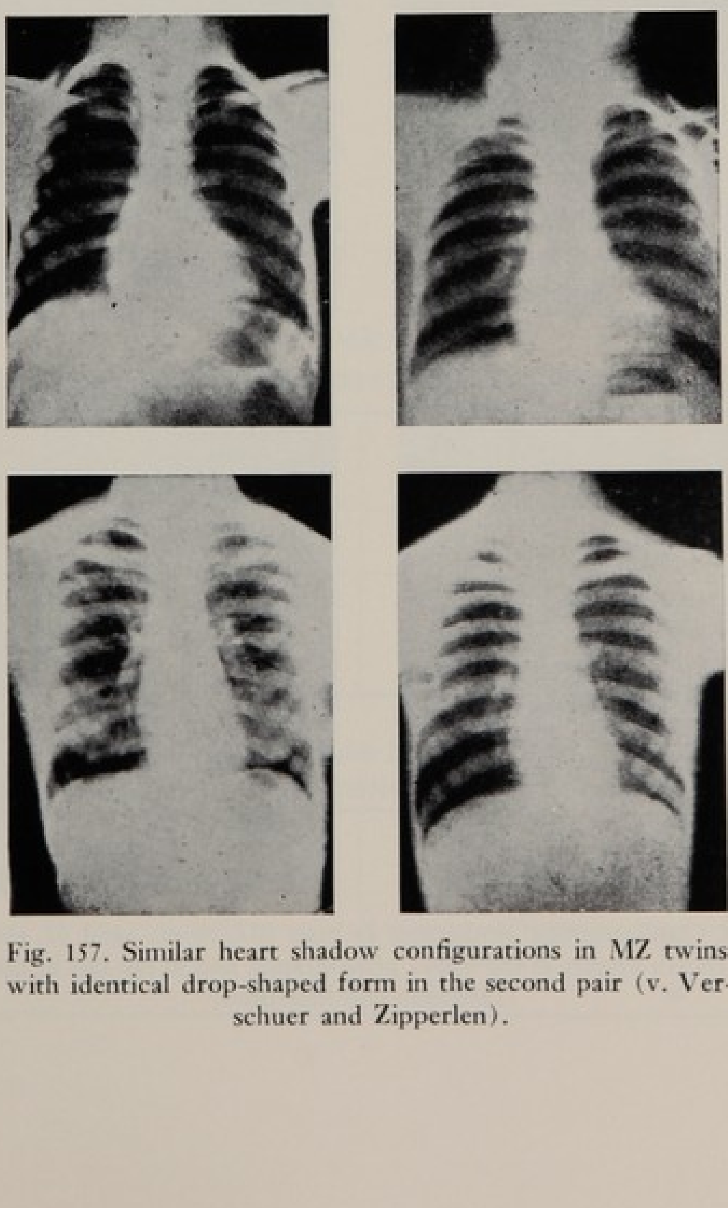


Fig. 157. Similar heart shadow configurations in MZ twins, with identical drop-shaped form in the second pair (v. Verschuer and Zipperlen).

Ogawa's (1939, 1940) investigations of Japanese twin fetuses. The extent of intra-pair similarity in one-egg twins as to the essentials of venous structures is exemplified by the author's findings shown in Plates X and XI (frontal branch of the superficial temporal vein).

The configuration of renal, mammary and cerebral blood vessels was investigated by Wagenseil (1930) in an aborted set of Chinese triplets of undetermined zygosity, by Yoskicka (1935) in a pair of one-egg twins, and by Higeta (1940) in twin fetuses. In a series of 90 MZ pairs, the morphology of skin vessels was examined by v. Verschuer (1933) in terms of the coloration of the cheeks, not only for the purpose of obtaining additional evidence for a zygosity diagnosis (as suggested by Siemens), but also for ascertaining such dermatological conditions as acrocyanosis and cutis marmorata. The analysis showed intra-pair similarity in 70 pairs, slight dissimilarities in 15 pairs, and considerable differences in 5

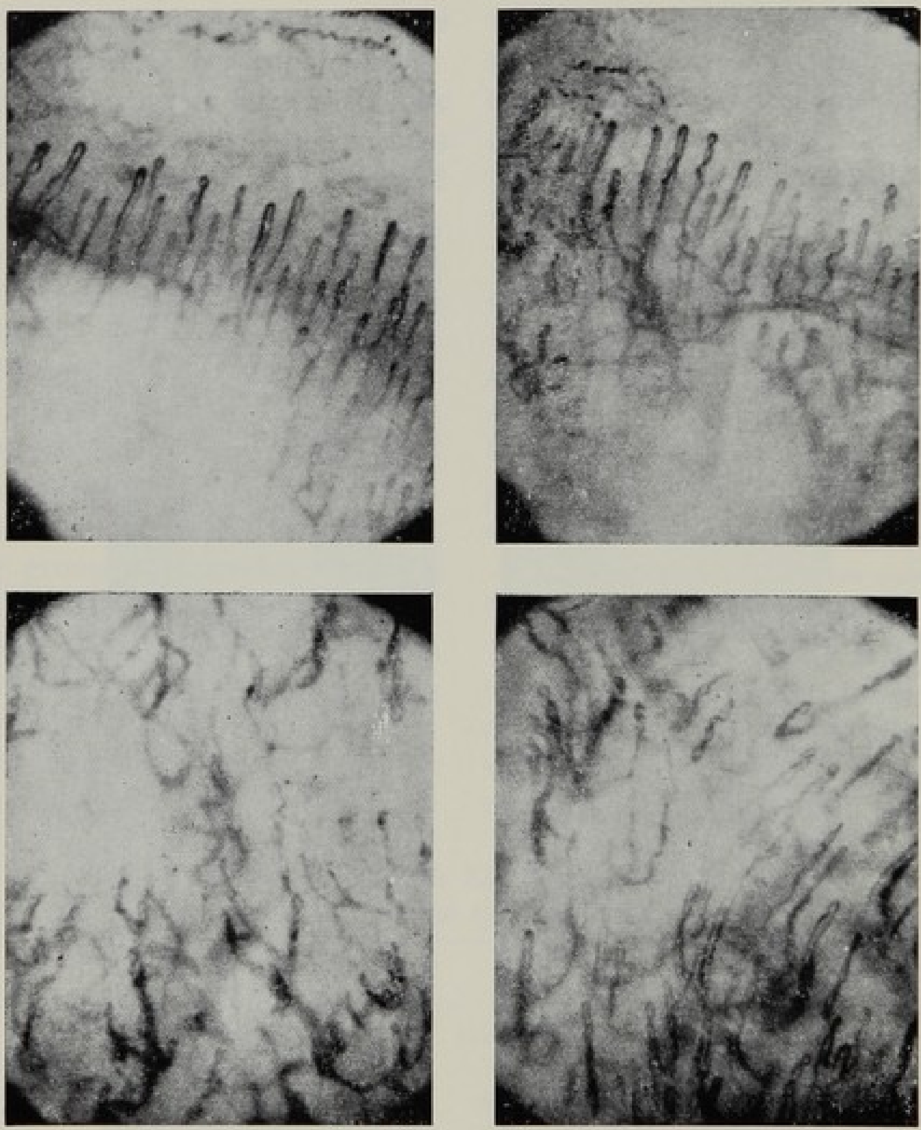


Fig. 158. Capillaroscopic similarities in male MZ twins, aged 63, shown in the left fourth fingers in the upper photographs, and in the lips in the lower (Lehmann and Hartlieb).

pairs, confirming the belief of Weitz, Curtius and Schokking that external factors responsible for tangible variations in the given characteristics are usually easy to identify.

Microscopic twin data on the structure of capillaries were gathered by Mayer-List and Hubner (1925), Lotting (1931), Schiller (1936) and others. The consensus was that there had been abundant evidence of a greater capillaroscopic intra-pair similarity in one-egg than two-egg twins. In Schiller's series of 80 MZ pairs, complete similarity was found in all pairs, not only with respect to capillary patterns, but also as to the volume of blood flow observed, while 27.7% of the two-egg pairs showed incomplete similarity, and the rest complete dissimilarity.

The capillaroscopic data of Lehmann and Hartlieb (1937), from a series of 50 MZ, 37 same-sex DZ and 13 opposite-sex pairs, were obtained from fingers and lips (Fig. 158). While 84% of one-egg pairs were classified as similar, over 90% of two-egg pairs showed intra-pair dissimilarities (Table L). The results of an analysis of the modifying effects of environmental factors are summarized in Table LI.

Apparently, the capillary structures of the majority of DZ pairs differed irrespectively of comparable environments, while those of most MZ pairs remained similar despite diverse living conditions (Figs. 159-162). Limited dissimilarities in one-egg pairs were ascribed by the investigators to such external influences as may be associated with occupational (electrician–baker), nutritional (well nourished – undernourished) or somatic differences (discordance as to congenital heart disease or similar pathological conditions).

Osato and Awano (1957) reported Igarashi's studies on similarity of the capillaries in 70 twin pairs (38 MZ, 17 same-sex and 15 opposite-sex DZ). The published tables of similarity percentages indicate very clearly that form and measurements of the capillaries are largely conditioned by heredity.

9. NERVOUS SYSTEM

Comparative data on the structure of the brain cortex were presented by Sana (1916)

Table L

CAPILLAROSCOPIC INTRA-PAIR VARIATIONS (LEHMANN AND HARTLIEB)

	Similarity		*Slight Dissimilarity*		*Marked Dissimilarity*	
	N	%	*N*	%	*N*	%
MZ	42	84.0	7	14.0	1	2.0
DZ Same-sex	1	2.7	13	35.1	23	62.2
Opposite-sex	1	7.7	2	15.4	10	76.9

Table LI

CAPILLARY STRUCTURE IN TWINS (LEHMANN AND HARTLIEB)

Capillary Structure	*Environment*	*Number of Pairs*	*MZ*	*DZ*
Similar	Different	8	6	2
Dissimilar	Equal	42	4	38

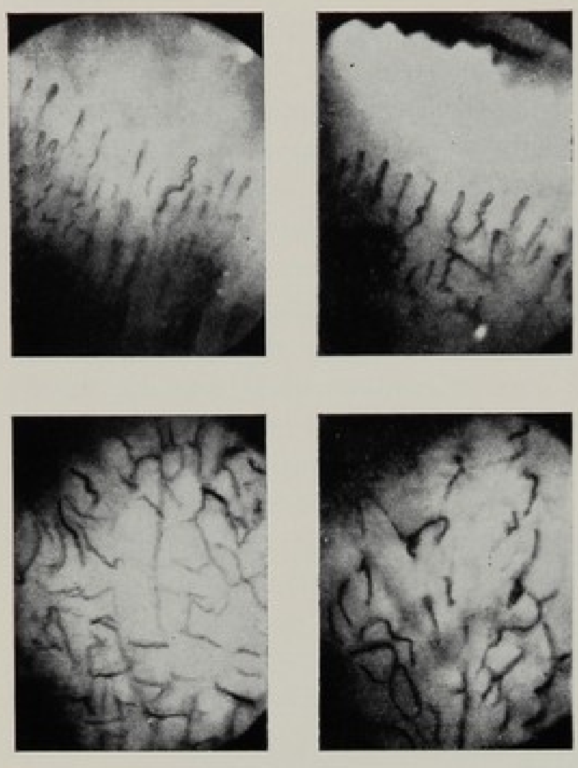


Fig. 159. Capillaroscopic similarities in 14-year-old male MZ twins (right fourth fingers and lips).

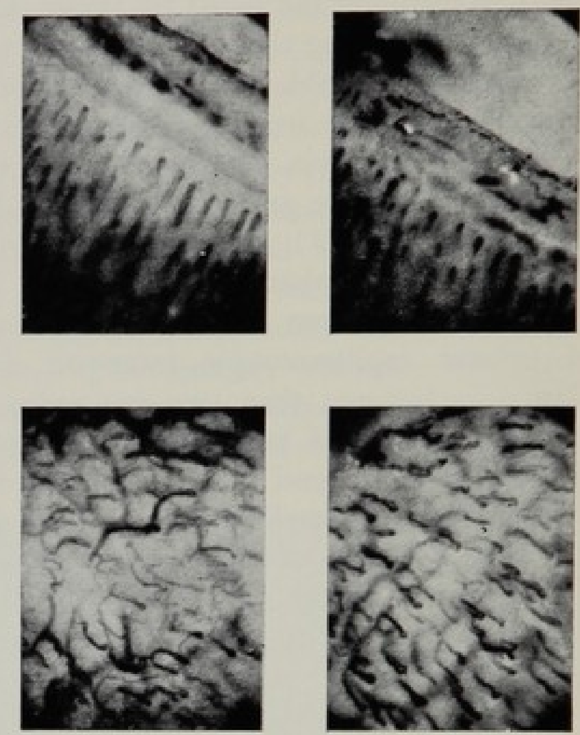


Fig. 160. Capillaroscopic similarities in 12-year-old male MZ twins (right index fingers and lips).

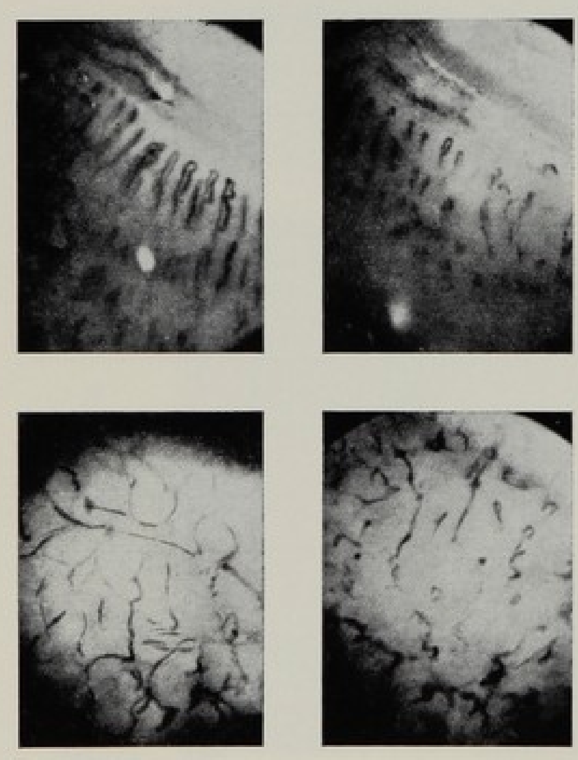


Fig. 161. Capillaroscopic dissimilarities in female DZ twins, aged 31 (right fourth fingers and lips).

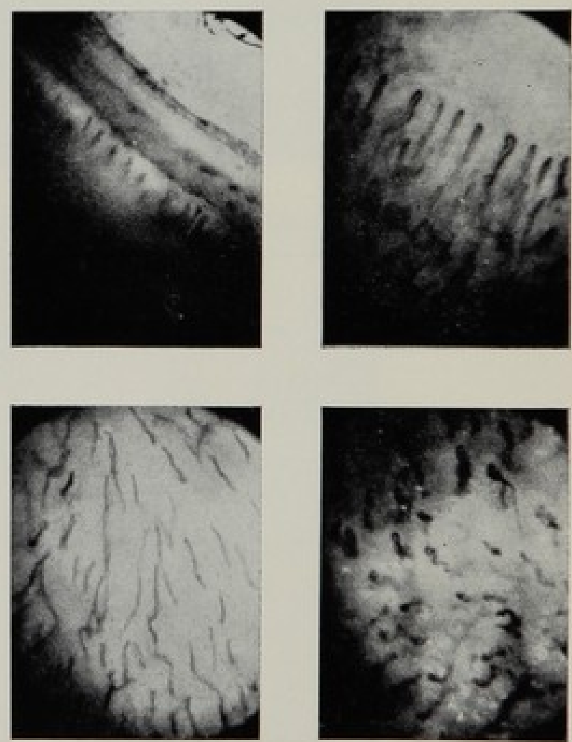


Fig. 162. Capillaroscopic dissimilarities in male DZ twins, aged 14 (right middle fingers and lips; Lehmann and Hartlieb).

Plates X and XI. Marked prominence of the superficial temporal vein (frontal branch) in a
of 8-year-old MZ twins (observed by Gedda)

Plate XI.

and Rössle (1937) on the basis of small series of twins, and by Wagenseil (1930) for a set of triplet fetuses (at various stages of cortical differentiation). However, the pieces of information made available by the twin study method in this important area have not been conclusive enough to warrant detailed description.

10. RESPIRATORY SYSTEM

The structure of the larynx was studied by Luchsinger (1944) in 29 MZ and 12 DZ pairs, both by measuring devices and laryngoscopically. Intra-pair similarity was observed in most one-egg pairs (20 and 26 pairs, respectively by the two methods) and, to some extent only, in four two-egg pairs. A common occurrence in DZ pairs was an entirely dissimilar projection of the Adam's apple, indicating different cartilaginous structures. Another interesting finding, ascribed to prenatal influences, was a laryngeal asymmetry in one member of a pair of one-egg twins concordant as to mental deficiency.

Intra-pair similarity as to various structural characteristics of the lungs was reported by Curtius and Korkhaus (1930) for 63% of MZ pairs and 18% of DZ pairs (Table LII). Also, similarly fused upper and middle lobes on the right side, with equal bronchial configurations corresponding to Heiss' second type, were described by Wagenseil (1931) in a set of triplets.

Table LII

CONFIGURATION OF LUNGS (CURTIUS AND KORKHAUS)

	MZ		*DZ*	
	No. of Pairs	*Per Cent*	*No. of Pairs*	*Per Cent*
Very similar	22	63.0	4	18.0
Moderately similar	11	30.5	11	51.0
Dissimilar	2	6.5	7	31.0
Total	35	100.	22	100.

Gedda, Bresadola and Volta (1957), in their previously reported study by means of transverse laminagrams, found that the shadow of pulmonary hili is more similar among MZ than DZ twins.

In a study on environmental variability of the chest and lungs, reported by Osato and Awano (1957), Yoshizumi and Ito found, on the basis of data from 130 twin pairs between 6 and 22 years of age (63 MZ, 45 same-sex and 22 opposite-sex DZ) that while both lung height and lung surface are only partly conditioned by heredity, the latter shows less environmental variability.

11. ABDOMEN

In the triplets studied by Wagenseil (1931) the right lobe of the liver was found divided in all three fetuses. On the other hand, only two triplets showed a lobule in the quadrate lobe, and one of them had two precaudate fissures (anterior and posterior) in addition. The third triplet had one posterior precaudate fissure. Another difference involved the branching of the vena cava.

Intra-pair similarity in one-egg twins was reported by Weitz (1924) and Morikawa (1938) as to form and size of the stomach, and by the latter investigator also with respect to the pyloric antrum and canal and the cardiac part of the stomach. While complete similarity was seen in the majority of one-egg twins, it never occurred in a two-egg pair.

More recently Osao and Awano (1957) reported Ito's researches on stomach shape by means of x-ray plates from 48 twin pairs (13 male and 11 female MZ; 11 male, 8 female and 5 opposite-sex DZ). Analyzing total findings for 16 traits, it appeared that the shape and measurements of the stomach are highly conditioned by heredity.

Renal structures in twins were studied by Yoskioka (1935) and Nagata (1938).

12. ENDOCRINE SYSTEM

Morphological characteristics of the thyroid were analyzed by Curtius and Korkhaus (1930) in a series of 42 MZ and 27 DZ pairs. These data, summarized in Table LIII, pointed to the operation of some genetic factor or factors in agreement with an earlier hypothesis of Siemens, v. Verschuer and Weitz.

Table LIII

DEVELOPMENTAL CHARACTERISTICS OF THE THYROID (CURTIUS AND KORKHAUS)

	MZ		*DZ*	
	No. of Pairs	*Per Cent*	*No. of Pairs*	*Per Cent*
Similarity	40	95.2	19	70.4
Slight similarity	1	2.4	5	18.5
Dissimilarity	1	2.4	3	11.1
Total	42	100	27	100

Both thyroid and thymus glands were studied by Wagenseil in the previously mentioned set of triplets and revealed various similarities and dissimilarities.

Quantitative twin data on the pituitary gland were reported by Mine (1937).

13. THE BLOOD

Of the constituents of the blood studied by Glatzel (1931) in an infant series of 44 MZ and 37 DZ pairs, it was chiefly erythrocytes, polynuclear neutrophils, monocytes and hemoglobin concentration that were found quantitatively to follow a genetically determined pattern. No such evidence was obtained for lymphocytes, eosinophils or basophils; nor, for that matter, for the total number of white blood cells.

Similar studies were carried out by Takahashi (reported by Osato and Awano, 1957) on erythrocyte size (from a material of 100 twin pairs) and on the proportion of blood constituents (from a material of 120 twin pairs). The published data indicate that erythrocyte size is largely conditioned by heredity, but also susceptible to environmental influences. While genetic conditioning could be shown in the hemogram and Elmogram, the influence of heredity could not be clearly appraised for blood platelet count and reticulocyte count.

The correlation between leucocytes and Arneth's formula was computed by Turpin in 62 MZ and 67 DZ pairs, first in collaboration with Piton and Caratzali (1939, 1941) and later with Bernyer (1947). The observed r values were .8 for one-egg and .42 for two-egg twins (.38 for same-sex and .53 for opposite-sex DZ pairs, but slightly higher than the correlation between ordinary siblings). The given variations were explained on a genetic basis.

Torrioli-Riggio and Reggiani (1956) studied Arneth's formula in 98 twin pairs (60 MZ, 38 DZ) and 2 triplet sets (one MZ and one DZ). Of the 60 MZ pairs, 39 were healthy, 11 were concordant as to disease and 10 were discordant as to disease. The authors found that in the formula's group I genetic factors had a limited influence while disease had a very marked influence. In the formula's other four groups the influence of genetic factors prevailed.

Early twin data on blood groups were published especially by Schiff (1914), Ottenberg (1922), Buchanan (1922), Mino and Garlasco (1923), Dyke and Budge (1929), and Schiff and v. Verschuer (1931, 1933). The consensus was that intra-pair similarity as to isoantigens distinguishes one-egg twins.

The most comprehensive studies were those of Schiff and v. Verschuer, who extended their work to the M and N factors, to the subgroups A_1 and A_2, and to the presence of group specific saliva substances. Their first series consisted of 73 MZ, 62 same-sex DZ, and 26 opposite-sex pairs, and the second of 202 MZ and 244 DZ pairs. Consistent intra-pair similarity as to all serological characteristics studied was shown in this material to be a highly specific feature of one-egg twins, while any dissimilarity undoubtedly meant dizygosity.

The distribution of intra-pair similarity and dissimilarity was the same in two-egg twins of the same or opposite sex and single born siblings, except for the A and B and M and N systems in regard to which the observed dissimilarities between two-egg twins were lower than statistically expected. Significant variations in isoantigens or other hematological characteristics due to external influences, including prenatal ones, were regarded as doubtful by the investigators.

In a similar study based on 67 MZ and 39 DZ pairs and 93 sets of full sibs, the present author (1951) obtained the following percentages for intra-pair similarity as to the presence of isoantigens: MZ twins . . . 100; DZ twins . . . 64; siblings . . . 58. Once again, two-egg twin partners proved to be slightly more similar than ordinary sibs.

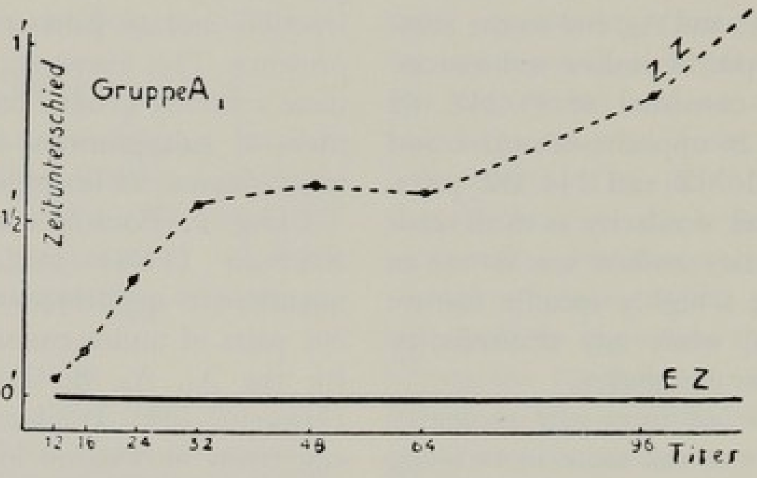
Quantitative analyses of isoagglutinins were carried out by Bühler (1935, 1940) in two series of twins, one consisting of 22 MZ and 18 DZ pairs, and the other of 150 MZ and 200 DZ pairs. Determinations of the agglutination titers for agglutinins α and β revealed intra-pair similarity in 120 MZ and 80 DZ pairs. In another study dealing with β fractions in 61 MZ and 74 DZ pairs, 26 sera were found to contain fraction β_1. The given twin subjects belonged to 7 MZ and 16 DZ pairs. In other words, of 61 one-egg pairs, three were alike as to the presence of the β_1 fraction, 54 were alike as to its absence, and four were unlike. In the two-egg group, 58 pairs were alike in lacking the β_1 fraction, and 16 pairs were unlike as to its presence. This distribution led Bühler to assume a strictly genetic basis for the different titers of isoagglutinins α and β and, to a lesser degree, of isoagglutinin β_1 as well.

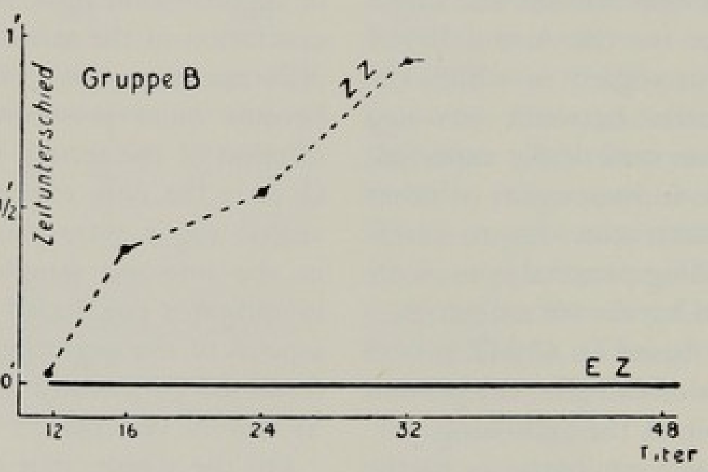
Using v. Ponsold's method, Ayres de Azevedo (1944) made qualitative and quantitative agglutination tests in a series of 201 pairs of undetermined zygosity, testing for the A_1, A_2, B, O, M and N factors (Figs. 163-166). While the red cells of one-egg twins showed no intra-pair differences in agglutination time, regardless of the concentration of the serum, there were distinct differences in the two-egg group, which became more pronounced with increasing dilution of the serum. Cells of blood group O were the only exception in that they revealed slight intra-pair dissimilarities even in the one-egg sample. At any rate, the investigator concluded that the quantitative aspects of the agglutination reaction are determined genetically in both the ABO and M and N systems.

On the whole, it is justifiable to state on the basis of all available twin data that one-egg twins have the same antigens in the stroma of their red cells. A rare exception ascribed to an abnormality in fetal development was Panagiotou's (1938) pair of apparently monozygotic twins, of whom only one showed evidence of antigen B inherited from the mother.

Another notable case, described by Schiff, concerned a set of triplets in whom blood group determinations led to a diagnosis of superfetation. With the mother belonging to group O, impregnation by two men was assumed, since neither a man belonging to groups A or B nor one belonging to group AB could possibly have fathered triplets falling into the three different blood groups reported.

Twin data on the Rh factor were pre-





Figs. 163 and 164. Hematological comparisons of MZ and DZ twins (Ayres de Azevedo), as to blood group A, in the upper diagram, and blood group B in the lower. Zeitunterschied= Intra-pair difference in agglutination time. Gruppe=Group. Faktor=Factor. ZZ=DZ. EZ=MZ.

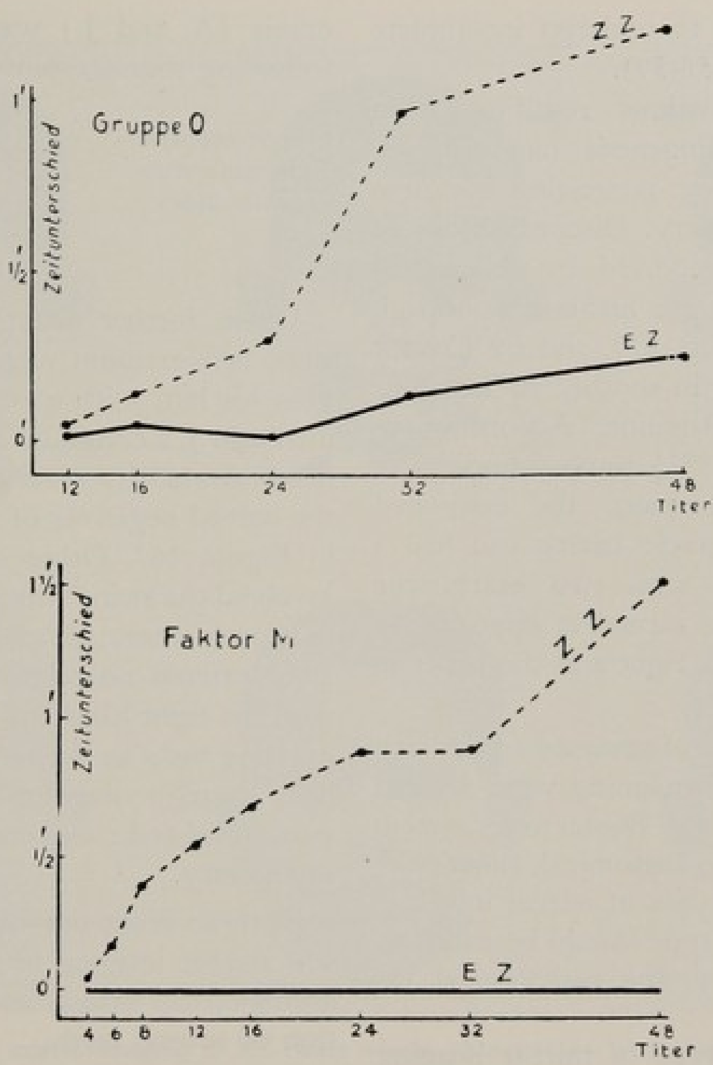
sented especially by Strandskov and Diederich (1945), although other studies will be cited in the chapter dealing with methodology. In the Chicago series, all 53 MZ pairs were either equally Rh+ or Rh—, while in the two egg group 59 pairs were equally Rh+, five pairs Rh—, and five pairs dissimilar.

More recently, studies on blood groups in twins have become the rule, in the sense that practically any twin research program includes blood grouping and typing as the first routine test of zygosity.

14. SPECULARITY (REVERSED ASYMMETRY)

In view of the fact that the phenomenon of specularity (mirror image, reversed asymmetry) has both anatomical and functional implications, it is of particular importance in the study of twins. Just as the image of an object reflected by a mirror reverses the two sides of the object, so it may happen in twin partners that they show signs of reversed laterality.

Specularity may involve asymmetrical



Figs. 165 and 166. Intra-pair agglutination differences, as to blood group 0 in the upper diagram, and blood factor M in the lower (Ayres de Azevedo). Zeitunterschied= Intra-pair difference in agglutination time. Gruppe= Group. Faktor=Factor. ZZ=DZ. EZ=MZ.

(occurring only on one side of a person) as well as symmetrical (occurring on both sides) characteristics. Accordingly, the given characteristic will either be found only on the opposite sides of two twins or, when distinguished by definite differences on the two sides of an individual, will show reversed differences of this kind in twin partners.

One of the earliest cases of specularity produced experimentally was that of Dareste (1877) who obtained a *situs inversus* by heating fertilized eggs on one side only. More recent experiments were carried out by Morgan on ascidian eggs which upon isolation of the first two blastomeres underwent gastrulation with signs of mirror imaging in the muscle cells of each blastomere. Equally successful were the previously mentioned experiments of Spemann (1901, 1903) who produced conjoined twins with asymmetrically reversed organs by inducing triton eggs to undergo incomplete duplication (Figs. 56-59).

Double malformations resulting from teratological gemellogenesis (see Chapter VII) provided many interesting instances of reversed asymmetry. Discordance as to dextrocardia was reported by Allen and Pancoast (1875) in the Siamese xiphopagi, Chang and Eng (Fig. 67), and by Chapot and Prevost (1901) in another xiphopagous pair, Mary and Rosaline. According to Küchenmeister's (1888) autopsy findings in two thoracopagous pairs, the conjoined twins shared a thoracic cavity and had a single pericardium with two hearts, the axes of which were turned in opposite directions (one to the right and the other to the left).

The various forms of reversed asymmetry observed in normal twinning were divided by Zazzo, according to Bouterwek's system of classification, into anatomical, functional, and psychological types of mirror imaging. However, a fourth type should be added to this scheme, namely, the pathological varieties.

The *anatomical* type of mirror imaging which involves various organs and organ structures was well exemplified by Ley's (1929) pair of one-egg twins who were concordant as to early total deafness, with multiple signs of reversed asymmetry in addition. The similar shape of the twins' crania (A. and J.) was evidenced by the following measurements:

	A.	*J.*
Largest cephalic circumference	53 cm.	52 cm.
Cephalic index	$\frac{15.6}{17.2}=0.907$	$\frac{15.6}{17.3}=0.902$

Upon further scrutiny, however, A.'s right hemicranium was found to be larger than his left, with a reversal of this asymmetry in J.'s cranium. This specularity was demonstrated by reversing and remounting the halved negatives of photographs shown in Figure 167. Other signs of specularity involved the twins' fingerprints and handedness preference. Although both twins were ambidextrous on relatively simple tasks, J. used the right hand and A. the left for such exacting tasks as the farthest throwing of a ball, thereby showing a combination of anatomical and functional forms of reversed asymmetry.

In three other one-egg pairs, this author saw mirror imaging in the development of asymmetrical breasts and in the first dentition of several teeth.

Specularity in the hair whorl, which is clockwise in 74.5% and counterclockwise in 25.5% of the German population, was studied by v. Verschuer (1949) in a series of 163 MZ pairs. The following distribution was observed in this analysis:

Characteristic	*Observed*	*Theoretical Supposition (with 3 sigma limits)*
Counterclockwise whorl in both twins	58.9%	55.5±3×3.9%
Counterclockwise whorl in one twin and clockwise whorl in the other	31.3%	38.0±3×3.8%
Clockwise whorl in both twins	9.8%	6.5±3×1.8%

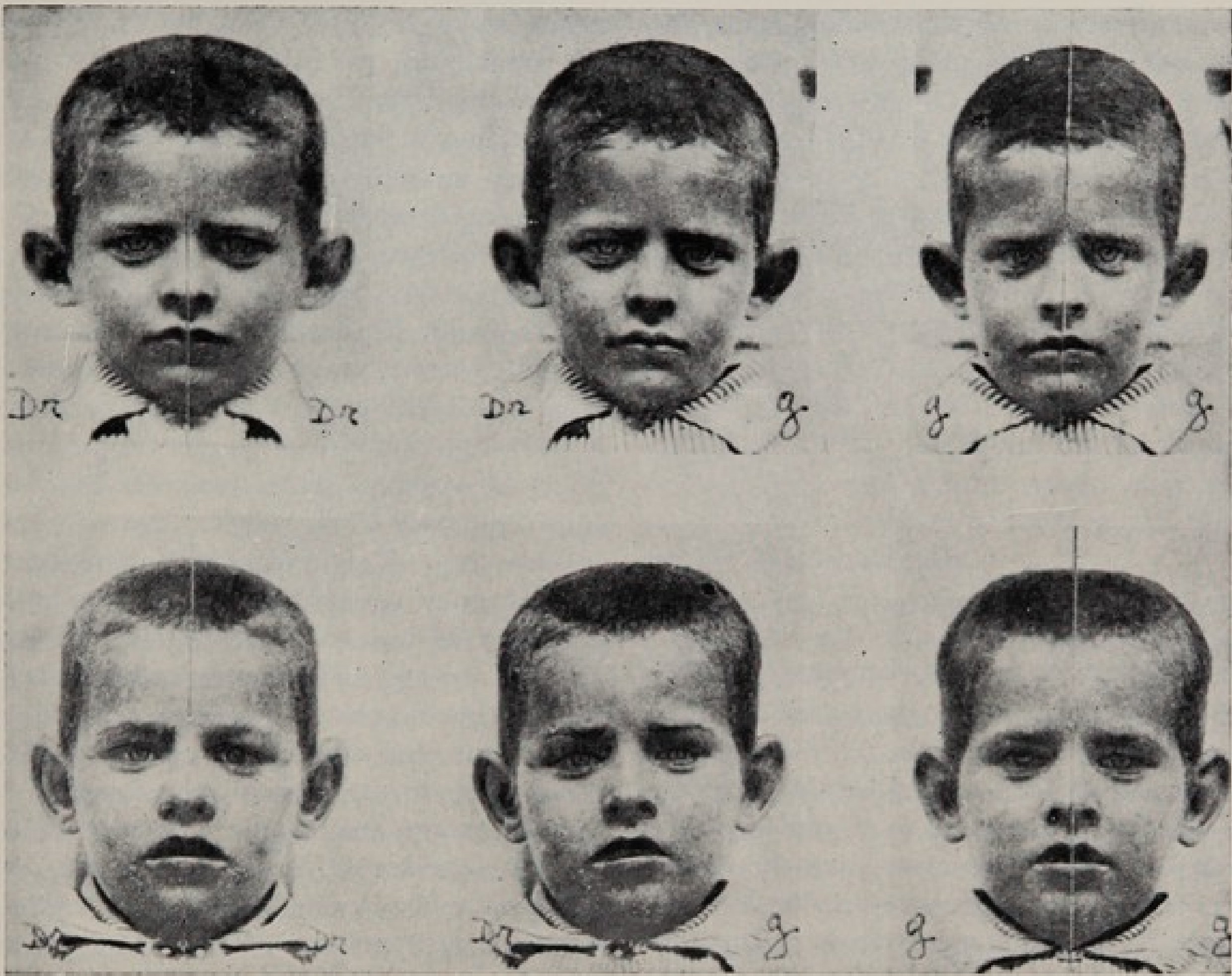


Fig. 167. Hemicranial mirror-imaging in MZ twins whose photographs were halved, reversed and remounted; original photographs in the middle, conjoined right halves on the left, and conjoined left halves on the right (Ley).

Hence, twins showed no statistically significant deviation from the random distribution of this generally asymmetrical characteristic.

Among the most striking instances of anatomical specularity in one-egg twins is completely or incompletely reversed asymmetry of the viscera as reported by Miller (1893), Araki (1935), Cockayne (1940), Newman (1940) and others. In Araki's Japanese pair, whose father had a set of normal twins among the children of his second wife, one twin showed total *situs inversus viscerum* (verified by x-rays and electrocardiogram), in addition to left-handedness and *scrotal situs inversus*, while the other twin was normally developed as well as right-handed. According to Newman (1940), only five cases of separate one-egg human twins had been reported as exhibiting s.i.v. in one of the twin partners. He also stated that these conditions were discovered mainly during autopsies of stillborn twins or of those that died in early infancy.

The genetic aspects of *situs inversus viscerum* in relation to twinning were investigated by Mattisson (1933) in families which included a case with this type of specularity (Table LIV). While twin births were not increased in these families, the proportion of MZ pairs seemed to be higher than expected (50% instead of the expected 25 .... 30%, according to Weinberg's differential method). It was assumed, therefore, that there might be a relationship between s.i.v. and one-egg twinning, although the need for a statistically representative sample was clearly acknowledged.

Table LIV

SITUS INVERSUS VISCERUM IN TWINS (MATTISSON)

Kindred	*No. of Individuals*	*Twin Births*	*Opposite-sex Pairs*	*Same-sex Pairs*
I	245	2	—	2
II	62	1	—	1
III	122	2	1	1
IV	194	3	1	2
Total No.	623	8	2	6

A special form of *situs inversus* is called isolated congenital dextrocardia when only the heart is involved. One-egg twin pairs with this type of mirror imaging were reported by Schott (1891), Paltauf (1901) and Ostertag and Spaich (1935). While Schott's observations were made in 45-year-old male twins, and those of Paltauf in twin fetuses, the twin sisters described by Ostertag and Spaich were 28 years old and distinguished by the fact that the dextrocardiac twin was an excellent sportswoman and athletically more proficient than her cotwin.

In the *functional* form of mirror imaging, one twin partner is seen to use the left side of the body for certain voluntary movements, while the other twin uses the customary right side. Referring chiefly to left-handedness, the phenomenon also applied to the preferred use of the left eye, of the left foot in kicking, of the left half of the body in swimming, of the left side in masticating or smiling, and the like.

As to handedness specularity in twins, Siemens (1924) as well as Lauterbach (1925) believed that left-handedness and twinning were causally related. In Siemens' series of 37 MZ pairs, 1 pair was left-left, 26 pairs right-right, and 10 pairs right-left. Of 31 DZ pairs, 2 pairs were left-left, 16 right-right, and 13 right-left.

However, no significant differences in the frequency of left-handedness were observed by Wilson and Jones (1932) either between one-egg and two-egg twins or between twins in general and single born persons. With throwing and writing as the main criteria for determining this functional type of mirror imaging in a sample of 70 MZ, 69 same-sex DZ and 54 opposite-sex twin pairs and 521 single born subjects, the observed percentages of left-handedness were 5.5 ± 7% and 12.0 ± 2.2% in twins and 4.1 ± .6% and 6.5 ± .7% in nontwins respectively for throwing and writing. The one-egg group included 1 left-left, 56 right-right and 13 right-left pairs, while there were 2 left-left, 97 right-right and 24 right-left pairs in the two-egg group.

Another study of functional specularity was conducted by Komai and Fukuoka (1934) in a series of 118 MZ, 28 same-sex DZ and 17 opposite-sex pairs and in a comparable control group of Japanese children of school age. With six criteria for determining hand preference, and one criterion (football) for that of the foot, the preferred use of the left hand or foot was found to be more frequent in two-egg twins than in nontwins or one-egg twins. While the frequency in DZ twins ranged from 10 to

30%, the corresponding percentages in MZ twins and single born subjects were 11 and 10.

According to Rife's (1933, 1938, 1939, 1940) data on 369 twin pairs and 687 single born students and their families, the observed increase in the frequency of left-handedness in twins appeared to be explained by certain intra-pair differences rather than by the number of pairs with two left-handed members. While the families of nontwins (with a total of 3542 persons) yielded a left-handedness rate of 7.5%, the corresponding values for one-egg and two-egg twins were 11.4 and 15.4%.

More precisely, of 223 MZ pairs, 6 were left-left, 176 right-right, and 41 right-left; and of 146 DZ pairs, 3 were left-left, 104 right-right, and 39 right-left. On the other hand, the frequency of left-handedness among the parents and sibs of one-egg twins was significantly lower than that observed in the families of single born subjects, showing just the reverse of what might be expected if the same factors were responsible for left-handedness and twinning as assumed by Lauterbach.

Although unable to explain the reduced frequency of left-handedness in the families of MZ twins and the absence of a similar difference between the families of DZ twins and nontwins, Rife believed (despite admitted imperfections in handedness diagnosis) that left-handed persons are more likely than right-handed ones to give birth to a left-handed child. Even in twins, both one-egg and two-egg, pairs with mirror imaging in handedness have a significantly higher proportion of left-handed relatives than pairs with two right-handed members. However, since there is no evidence for an increased proportion of left-handers in families that have produced a pair of twins, it would seem that variations in handedness are quantitative (polygenic) in their mode of inheritance.

In order to explain left-handedness on this multi-factor basis, Rife hypothesized that many persons might be genotypically intermediate as to their handedness potentialities. Lacking a definite preference for right- or left-handedness, they are easily shifted in one direction or the other by outside influences. In twins, such external circumstances as peculiar positional arrangements or lack of space *in utero*, while having little or no effect on those whose hand preference for one or the other side is clearly determined genotypically, would often result in mirror imaging by shifting one twin toward left-handedness.

Accordingly, one-egg twins of a distinctly right- or left-handed variety are unlikely to show intra-pair differences (mirror imaging) in handedness; but two-egg twins distinguished by different genotypes are apt to display handedness specularity whenever they are genetically intermediate in their handedness potentialities and then are shiftable by environmental conditions.

In Zazzo's (1945) opinion, most MZ pairs show no handedness specularity, nor is there any significant difference in the proportion of left-handers between one-egg and two-egg twins. With a left-handedness rate of 16% in twins (Wilson and Jones), and with a similar rate in his control group of 500 single born subjects (even without considering their higher proportion of potential left-handers) 30% of randomly paired members of any population with a 16% rate of left-handers would be expected to present mirror imaging as to handedness. The corresponding proportion of specular pairs would be 20% if the general rate of left-handedness were 10%. Zazzo concluded, therefore, that twinning and random pairing yield "exactly the same proportions of mirror imaging."

In a study of handwriting in a series of

113 MZ and 160 DZ pairs of twins, Román-Goldzieher (1945) classified handedness according to certain directional characteristics in the style of writing. The results of this analysis (Table LV) placed approximately one-half of all twin subjects in the left-handed category, and a majority of

Table LV
DISTRIBUTION OF HANDEDNESS IN TWINS (ROMÁN-GOLDZIEHER)

Handedness	*MZ*		*DZ*	
	No. of Pairs	*Per Cent*	*No. of Pairs*	*Per Cent*
Right-right	16	14.	30	19.
Right-left	82	73.	95	59.
Left-left	15	13.	35	22.

pairs (73 and 59%, respectively) in the group of twins showing mirror imaging as to handedness.

According to Dahlberg's (1948) review of the subject, the proportion of left-handers among twins, although varying from one sample to another, seemed to be generally higher in MZ than in DZ pairs, with an intergroup difference of $4.2 \pm 1.1\%$. However, there should be no one-egg pair showing specularity in handedness "were left-handedness a trait inherited in the classical sense."

Analogizing from the observation of anatomical and functional modes of reversed asymmetry, some investigators speculated about the possible effects of a *psychological* type of mirror imaging. In line with Bouterwek's (1934, 1936, 1938) theory based on two series of 40 and 100 MZ pairs, right-handed twin partners were thought to be more vigorous and energetic, more logical in a masculine sense, and more artistically inclined than their left-handed cotwins, described as generally weaker, more sentimental, and more interested in the sciences. Similar psychological differences indicative of "mirror imaging" were observed by Graewe (1941), while Zazzo (1945) spoke of complementary rather than reversed personality characteristics. In Zazzo's opinion, left-handed people in a predominantly right-handed culture are discriminated against to such an extent that this disadvantage will have "an inevitable impact on their personality development."

Pathological forms of mirror imaging (reversed asymmetry in pathological conditions for which twin partners are concordant) are apparently as common as the anatomical and functional varieties and are probably due to similar causes. The given category is highly diversified and includes such etiologically different conditions as rachitic scoliosis, congenital torticollis (Isigkeit), unilateral exophthalmos (Engerth), congenital anomalies of the eye (Pillat), anisometropia (Jablonski, Münch, Waardenburg), pterygium and strabismus (Bodtke), phlebectasic or goitrous localizations (Curtius and Korkhaus, Krüger), inguinal hernia (Stransky), infantile paralysis (Hofmeier, Messeri), Dupuytren's contractures (Then Bergh), congenital malformations (Abelin), and so forth. Figure 168 shows a striking case of mirror imaging as to paralytic poliomyelitis, originally reported by Messeri.

Of the various hypotheses which were proposed to account for the still obscure phenomenon of mirror imaging in twins, Dahlberg's (1926, 1929, 1943, 1948) explanation of asymmetrical genotypical influences due to positional changes in the process of inheritance was based in part on Przibram's (1908) breeding experiments with heterochromous Angora cats (yellow and blue eye colors). When cats with one yellow and one blue eye were mated with symmetrically blue-eyed or yellow-eyed

Fig. 168. Reversed asymmetry in MZ twins concordant as to paralytic poliomyelitis (Messeri).

animals, some of the offspring were heterochromous in turn, while others had two blue or two yellow eyes.

Dahlberg observed that it is generally believed that pigmentation in the stroma of the iris is inherited in animals as well as in man, and hardly influenced by environmental factors. This makes it very unlikely that the observed asymmetry may be due to some environmental influence before or after birth, which would also have recurred in three successive generations.

Przibram's finding that a parent with a blue right eye and brown left eye could father descendants with brown right eyes and blue left eyes indicated that a genotypic asymmetry may be expected to switch through the generations from the right to the left side or viceversa.

In another approach, Dahlberg (1948) used an analogy with the genetics of dextral and sinistral coiling in the water snail, *Limnaea peregra* (Fig. 169). With a maternally transmitted recessive gene apparently responsible for dextral coiling, the Swedish scientist postulated genotypically determined forms of reversed asymmetry even in one-egg twins, despite their genetic identicalness. His scheme explaining mirror imaging as to handedness ("motor asymmetry") is presented in Figure 170. If one imagines that, during the development of MZ twins, an asymmetrical organization of one twin can be transmitted to the other—possibly by means of some connection between the germinal layers, which later disappears—and the position of the twins is such that the cephalic extremities face in opposite directions, one may thus realize that all this could cause a reversal of the asymmetry of the

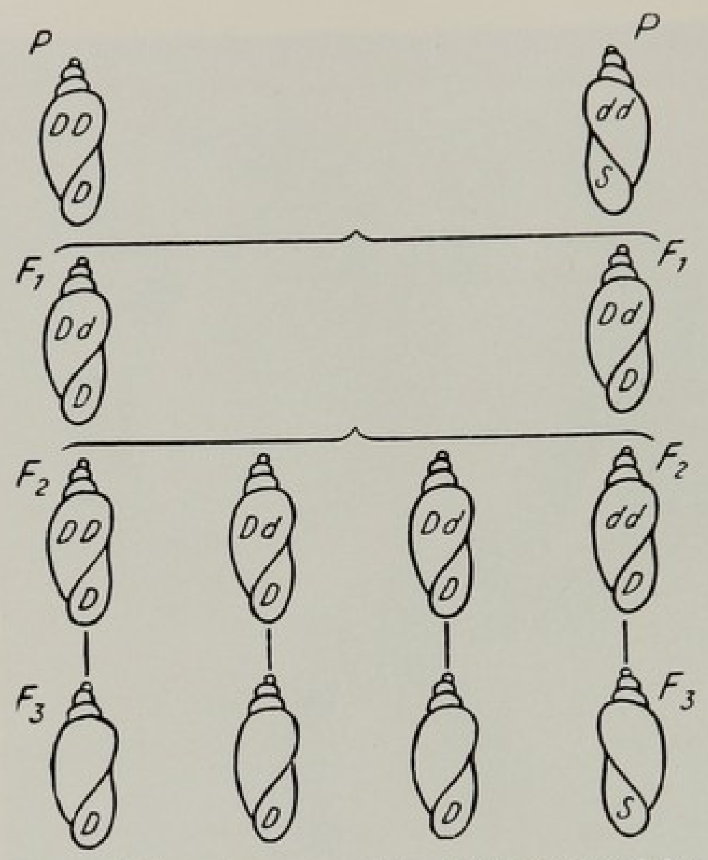


Fig. 169. Schematic representation of inheritance of dextral and sinistral coiling in the water snail (Dahlberg).

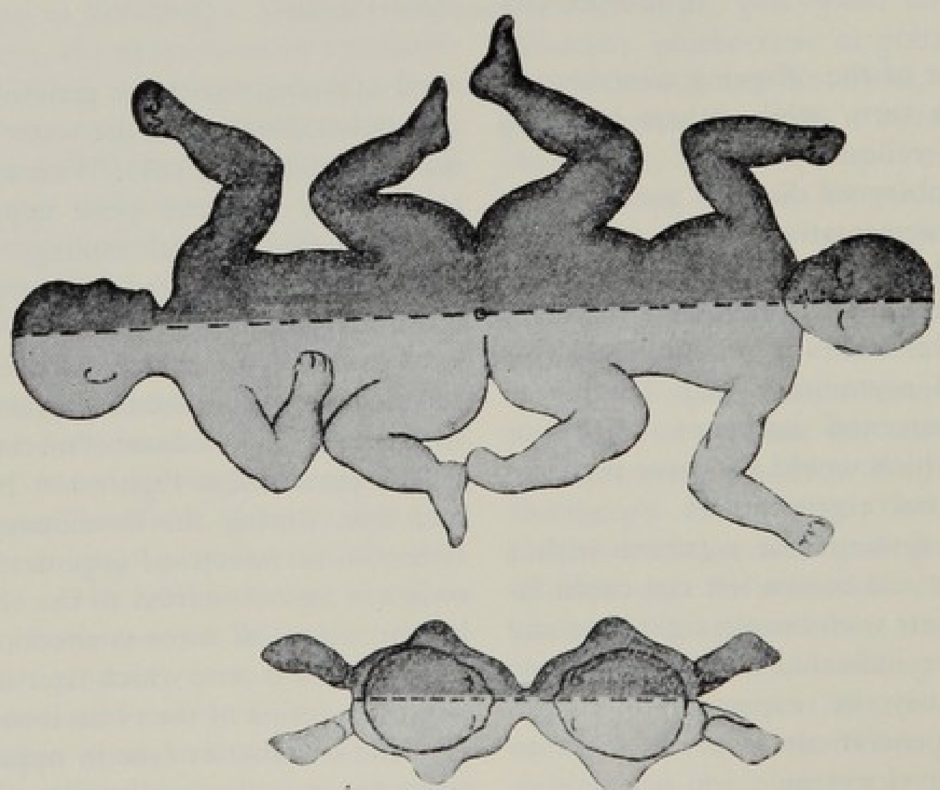


Fig. 170. Schematic representation of motor asymmetry (Dahlberg).

Fig. 171. Group picture of MZ and DZ pairs, including the conjoined Godena twins, Lucio and Simplicio, showing no greater similarity than ordinary MZ twins (Newman).

genotype, and so, because of their reciprocal position, the one twin becomes right-handed and the other left-handed.

As to the various combinations which may be observed in twins with respect to a specular trait, Dahlberg (1929) differentiated the following: (a) in both twins on the same side; (b) in the two twins on opposite sides; (c) on both sides in one twin, and on neither side in the other; (d) on both sides in one twin and on one side in the other; and (e) on one side in one twin.

According to Newman's (1928) findings on reversed asymmetry in twins (50 MZ pairs), there was some negative relation between degrees of intra-pair resemblance and the frequency of mirror imaging, inasmuch as twins resembling each other most closely were found to be least inclined to show mirror imaging. The same investigator (1931) observed that right-handedness was usually associated with a sinistral whorl of the hair, and vice versa, and that the right-sided partner of conjoined twins was always the one who had a larger head and face. In the Godena twins (Fig. 171), for instance, Simplicio on the right was brachycephalic, and Lucio dolichocephalic.

Since a similar variation may exist between the right- and left-handed members of ordinary one-egg pairs, Newman assumed that a right-handed twin with a larger head and face always originated from the right half of the zygote. He also believed that one-egg twins (including conjoined and monstrously malformed ones) may range from most similar to least similar pairs.

This hypothesis was based on the assumption that when twinning occurs before gastrulation, the two halves are of equal potentialities. Such twins will be virtually identical and show no signs of reversed asymmetry. However, with the division of the zygote taking place during gastrulation, that is, at a time when bilateral symmetry has already been established, the two halves are sufficiently differentiated to produce a right and a left side of the organism. The more advanced the formation of bilateral symmetry at the time of division, the less likely that the original state of equipotentiality can be reestablished.

With both halves producing a complete individual in more or less advanced stages of symmetry in development, signs of reversed asymmetry in a given pair will be present to a correspondingly greater or lesser extent. Were division to take place at so late a stage of development as to remain incomplete (double malformations), various differences between the two organisms would be expected, since both halves are already differentiated with respect to the right and left sides. Therefore, Siamese twins are less apt to be exactly alike than ordinary one-egg twins.

In another explanation based on Komai's experiments on over 1,000 salmon embryos, Newman emphasized that the frequency of *situs inversus viscerum* had been found to be higher in separate twin embryos than in nontwin embryos, while that in conjoined embryos in turn exceeded the rate observed in separate one-egg twins. The given intergroup differences were ascribed to a common denominator such as retarded development due to external causes. On the whole, it was assumed on the basis of available experimental data that abnormal outside factors might be responsible not only for s.i.v. in nontwins, but also for twinning itself and such phenomena in twins as mirror imaging, deformities, developmental retardation and double malformations.

It is justifiable to conclude, therefore, that the overall problem of reversed asymmetry in twins has not yet been adequately explained. The theories offered vary from entirely extrinsic (Newman) to strictly genetic (Dahlberg) modes of causation. The prevailing view would seem to be, however, that both endogenous and environmental factors may be at work. This hypothesis is epitomized by Rife's explanation of hand preference (motor asymmetry).

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