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Istituto di Genetica Medica e Gemellologia « G. Mendel », Roma (Italia)
(Direttore: Prof. L. Gedda)

The Contribution of the « Clinical Twin Method » to the Study of Sex Anomalies in Childhood*

(Phimosis, hypospadias, cryptorchism, adiposogenital dystrophy Laurence-Moon-Bardet-Biedl syndrome)

L. Gedda, F. Di Raimondo

The Twin Method for the study of the problems both of Human and of Medical Genetics generally develops by means of a comparison between the two series of twins, the monozygotic and the dizygotic. This classical method which we shall call « Interzygotic Twin Method » obviously requires more than one case.

At the XI International Congress of Genetics (1963) one of the Authors proposed a method whereby the members of a monozygotic twin pair sufficed to permit a mathematical analysis of a morbid phenomenon and to deduct conclusions referring to Genetics and Pathology.

While we refer to the original text for what concerns the details (10), we limit ourselves to point out that the statistical analysis in this method is based on the following general principle: every individual with his normal and pathological characteristics represents a statistical universe permitting a significant comparison between co-twins; besides, such a method is based on the principle of the transition from the macro- to the micro-clinical diagnostic picture of carefully listed and discriminated symptoms.

This one-pair method is called Clinical Twin Method, and we shall refer to it, prevalently but not exclusively, in presenting a series of cases of malformations of the sex apparatus in twins which belong to the Twin Register of the Mendel Institute, Rome.

* Lecture read at the Symposium on « Sex Pathology in Childhood » held at Perugia (Italy) on May 9-11, 1964.

We have limited this series to the male sex, because in our material males offer a more evident pathology, and also more varied and perhaps more numerous examples during the prepuberal period.

In the first place we shall examine a number of cases concerning phimosis, which is clinically not a serious malformation and is therefore little studied, although rather frequent. Curtius and Korkhaus (1930) described a MZ pair discordant as to phimosis; Brauns (1934) and Turpin (1938) each reported a MZ concordant pair.

From a random sample of our Twin Register we have drawn a number of affected male twin cases (cfr. Tab. 1).

Tab. 1. Phimosis in twins

	No. of twin-pairs	Concordant		Discordant	
		no.	%	no.	%
MZ	9	8	89	1	11
DZ	12	4	33	8	67
Total no.	21	12		9	

A comparison according to the Interzygotic Twin Method repeats the classical pattern of higher *concordance* in the monozygotic series (8 out of 9 cases, or 89% of concordance) and higher *discordance* in the dizygotic series (8 out of 12 case, or 67% of discordance).

Calculating the χ^2 with Yates' correction for the weak frequency classes, we obtain a value of 3.41 with a probability of random occurrence of 6.52 per cent. This value is slight enough to make improbable the hypothesis of independence of the concordance of phimosis from the zygotic condition.

Applying Huizinga's modified method (11), in the hypothesis of a monomeric diallelic trait, for a gene frequency ranging from 0.01 to 0.02, the penetrance of the pathological genotype can be established at between 0.9 and 0.8. Obviously we could not take into account opposite-sexed pairs with phimosis because this is a case of sex-limited inheritance.

Coming to the Clinical Twin Method we shall pick some cases from the above-mentioned material and examine them one by one.

Case 1, MZ, aged 2 (Fig. 1). They present the same four symptoms of phimosis (Figs. 2, 3), i.e. — besides preputial inflammation — scrotum slightly less developed than normal, testes reduced in volume, shiftability of testes up to the inguinal canal.

According to the Clinical Twin Method, one has to calculate the probability of random concomitance of the symptoms in the twins. The rejection of the random incidence is even more logical in our special case, inasmuch as considering the 4 concordant symptoms as being mutually independent, and admitting their presence or absence to be equally probable, we obtain p = 0.39 per cent. With the Clinical

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Twin Method it is possible to demonstrate that the two considered phimoses have a causal etiology that may logically be referred to the same genotype. In this pair further evidence is supplied by genealogical research; in fact we have also found a 3 year-old affected sibling (Figs. 4, 5, 6).

Case 2, MZ, aged 3, with concordant phimosis, could offer the occasion for a discussion as in the previous case, but we shall limit ourselves to show the photographs in order to demonstrate the details of the proboscis-like prepuce that repeats itself stereotypically in both, due to their identical heredity (Figs. 7, 8, 9).

Case 3, DZ, aged 14, concordant as to phimosis (Figs. 10, 11, 12). The malformation is concordant, being present in both, but different. And this fact corresponds to the presence of a 50 per cent different genotype.

Finally, we report two genealogical trees of female twins, obviously without phimosis, whose father and brother were affected (Figs. 13, 14). We have here genealogical non-twin contributions to the heredity of phimosis.

Let us now proceed to consider another urogenital malformation unit in pediatric age and in twin-cases, i.e. hypospadias.

The literature on the subject contains 15 concordant MZ pairs (Rumpel, 1921; Kermauner, 1924; Siemens, 1924; Voûte, 1933; Lehmann, 1936; Steiner, 1936; Camerer, 1938; Lamy, 1952, three pairs; Søerensen, 1953, five pairs); 8 discordant MZ pairs (Lehmann, 1936; Lamy, 1952, three pairs; Søerensen, 1953, four pairs); and 6 discordant DZ pairs (Lamy, 1952, four pairs; Søerensen, 1953, two pairs). According to Gregg (1941) hypospadias is a malformation that could be produced in the foetus by a rubeola of the pregnant mother.

Case 4, MZ, aged two months (Fig. 15), with balanitic hypospadias, i.e. the urinary meatus shifted to the level of the balanopreputial groove (Fig. 16), as also shown by this urinary jet which our photographer was able to snap and which, in some way, recalls a famous sculpture in Brussels.

The details of this urinary meatus identical in both is shown in Fig. 17. Their genealogical tree did not show any other case of hypospadias.

Case 5, MZ, aged 3, showing the urinary meatus where the balanopreputial groove would have to be (Figs. 18, 19, 20). The malformation is clinically slight, but complex, because the balanopreputial groove is missing in both twins. Moreover, in the first-born, the penis is curved and deviated towards the right, while in the second-born it is curved and deviated towards the left. Besides, in both, the penile cutis continues directly into the epithelium of the glans penis, without introflection of the preputial sac. The genealogical tree does not show other cases of hypospadias.

Case 6, DZ, aged 8 where only the second-born presents hypospadias, is also reported (Figs. 21, 22, 23).

Which deductions may we draw from these three cases of hypospadias in pediatric age? We shall follow the Clinical Twin Method. The fact that Case 4 is concordant not only as to hypospadias, but also as to the balanitic location of the urinary meatus with respect to the balanopreputial groove, brings the probability of random concordance to $p = 10.38$ per cent. On this basis we could not yet exclude

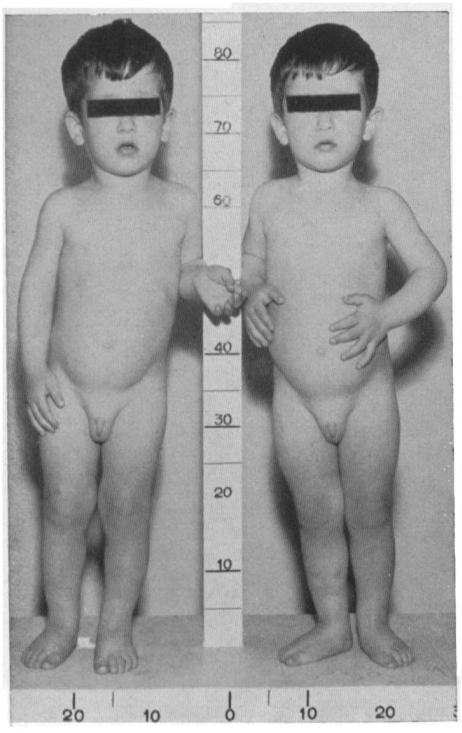


Fig. 1

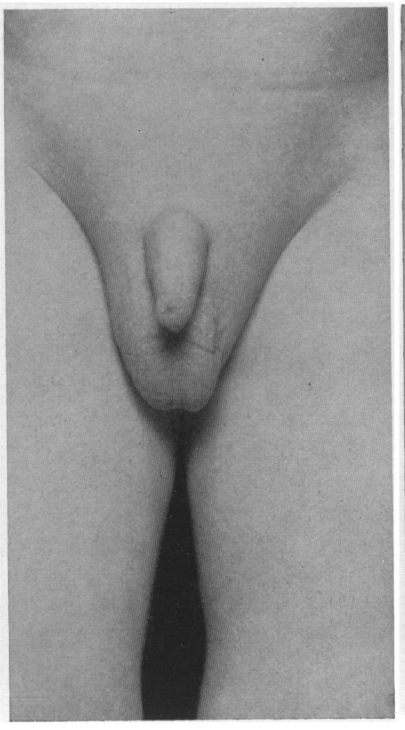


Fig. 2

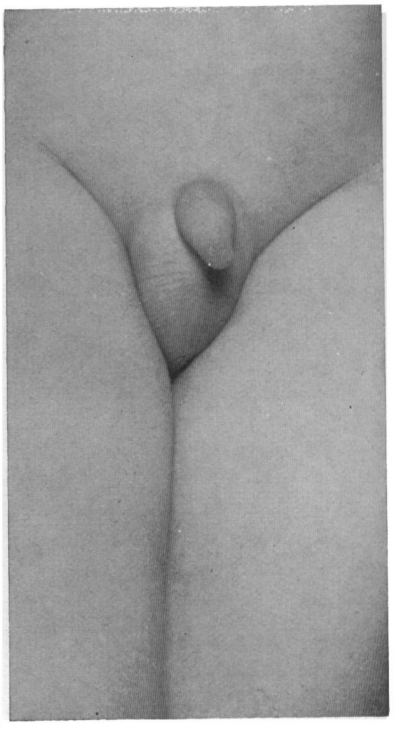
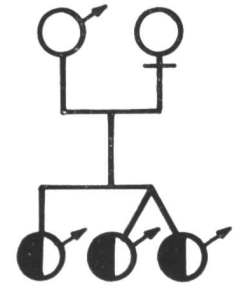


Fig. 3



PHIMOSIS

Fig. 4

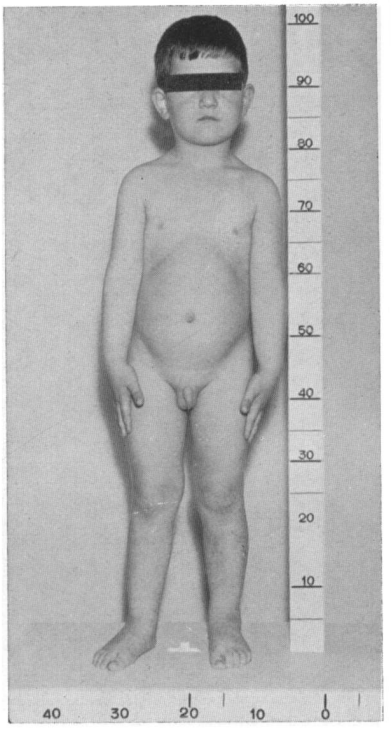


Fig. 5

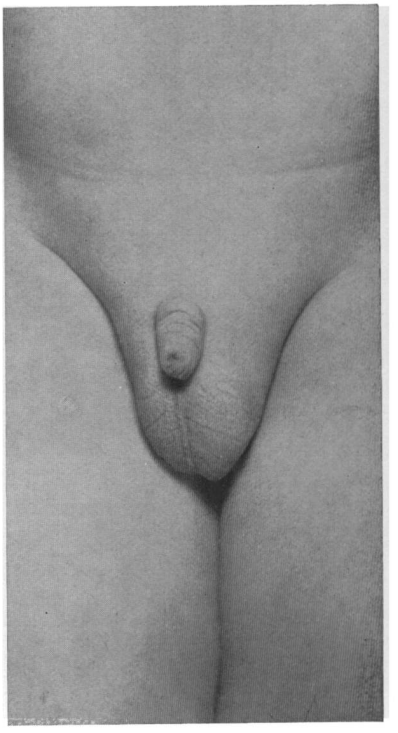


Fig. 6

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CASE 2

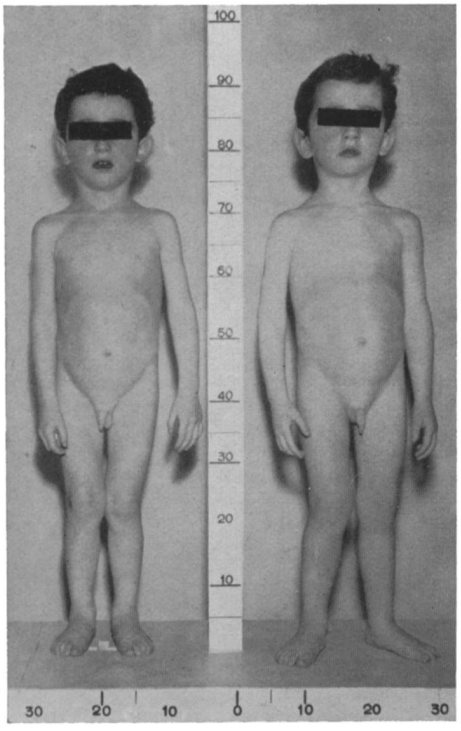

Fig. 7

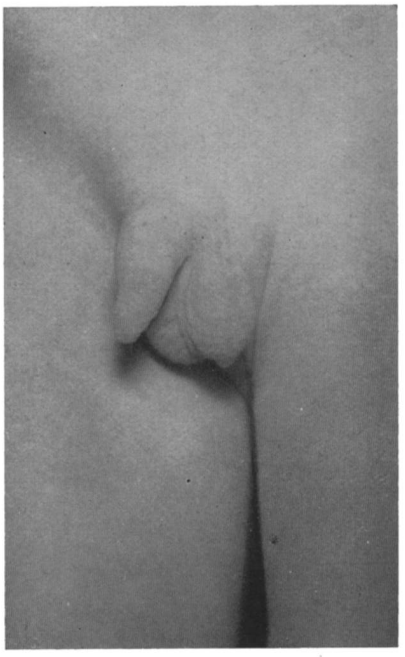

Fig 8

Fig. 9

CASE 3

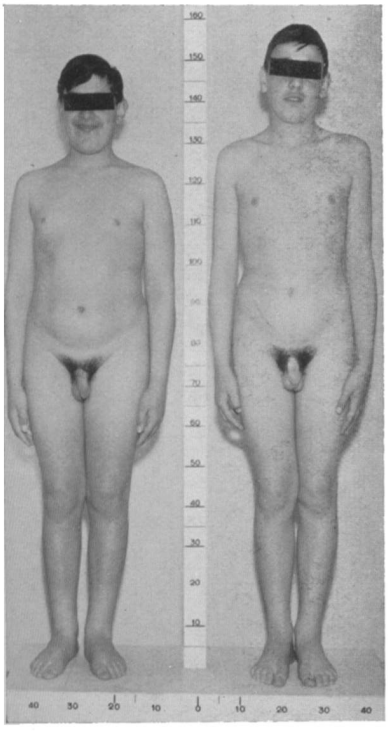

Fig. 10

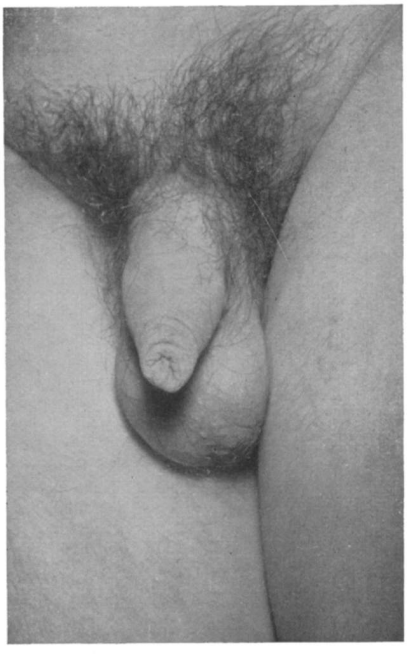

Fig. 11

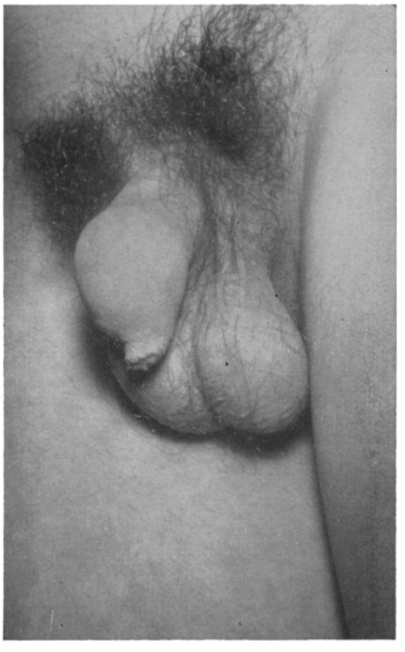

Fig. 12

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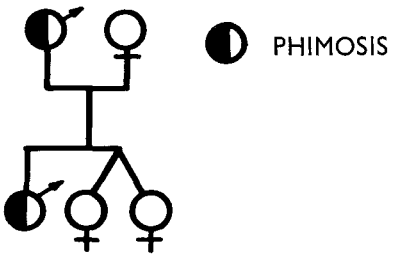

Fig. 13

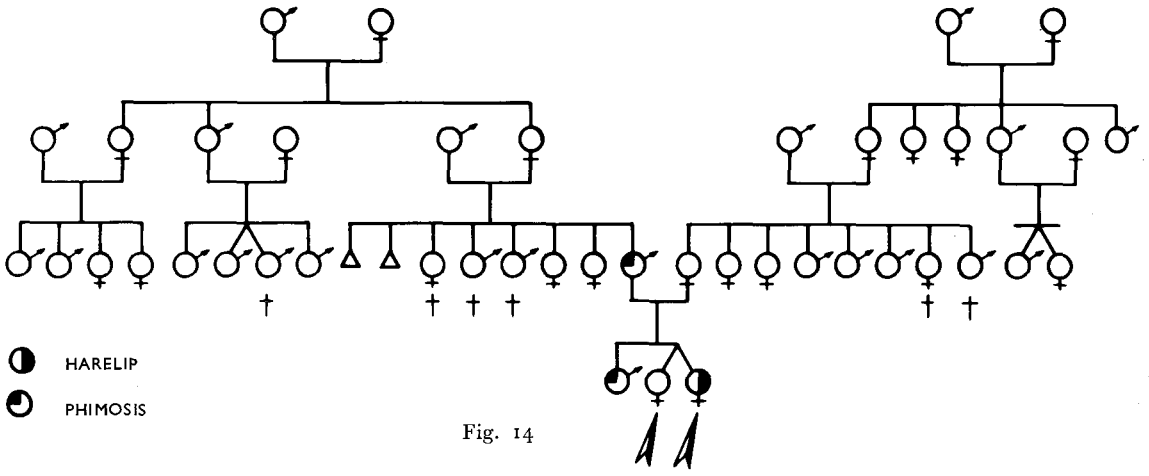

Fig. 14

CASE 4

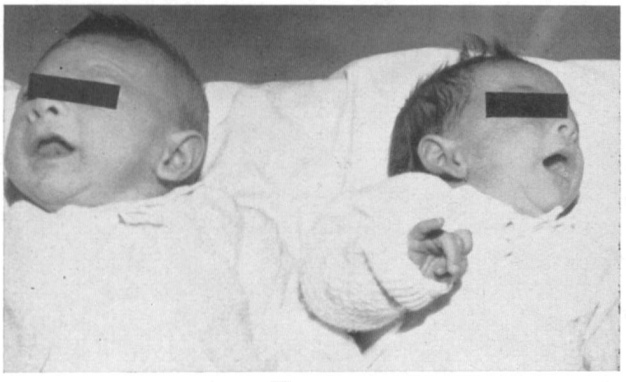

Fig. 15

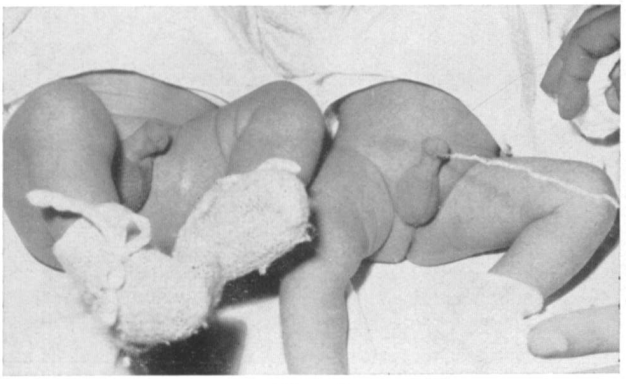

Fig. 16

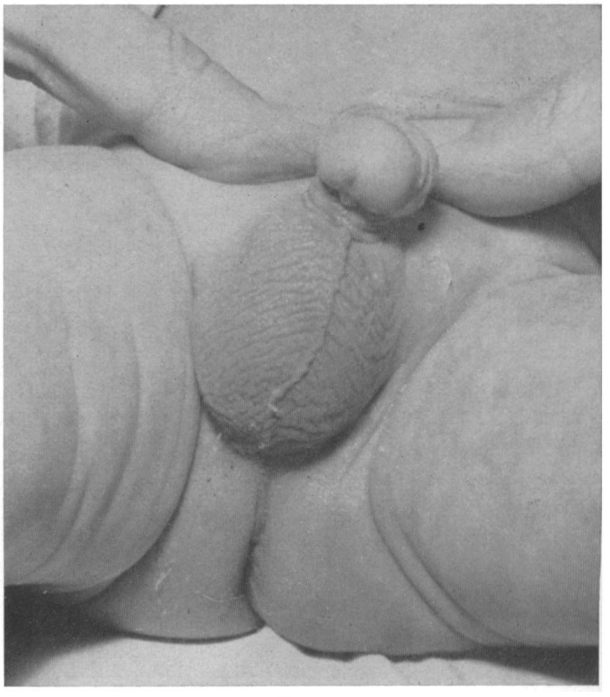

Fig. 17

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CASE 5

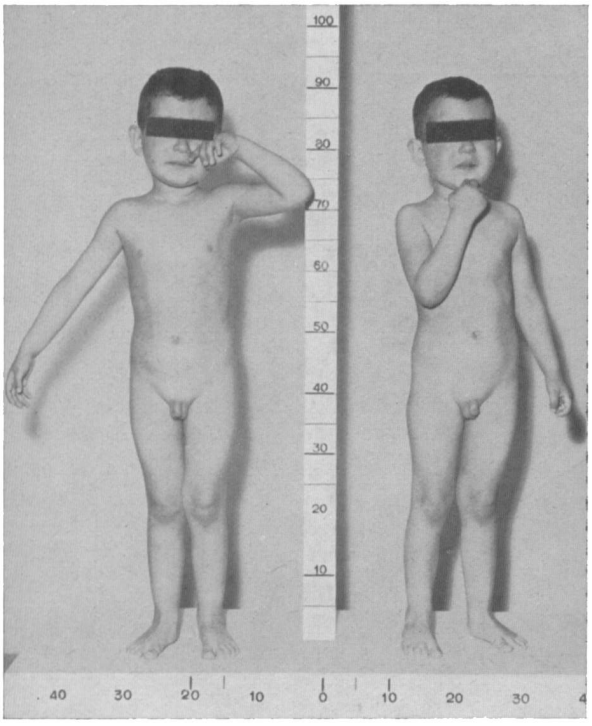

Fig. 18

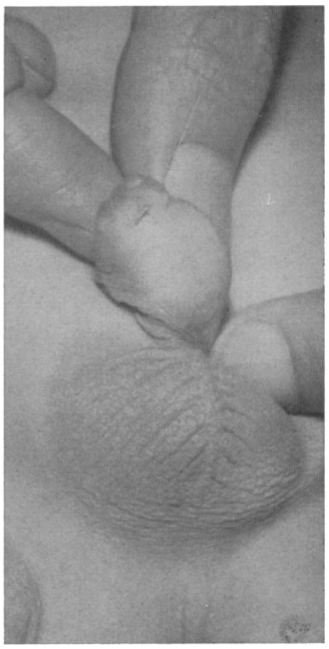

Fig. 19

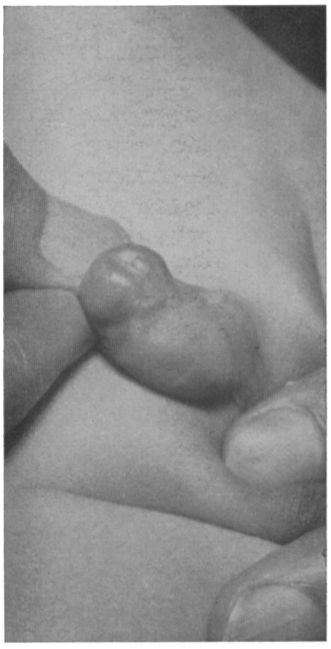

Fig. 20

CASE 6

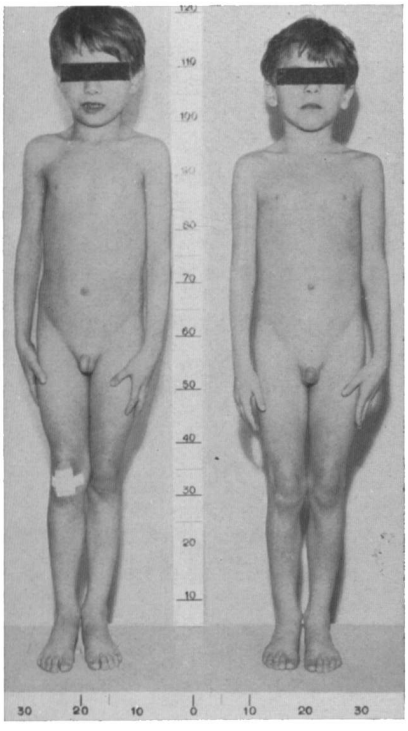

Fig. 21

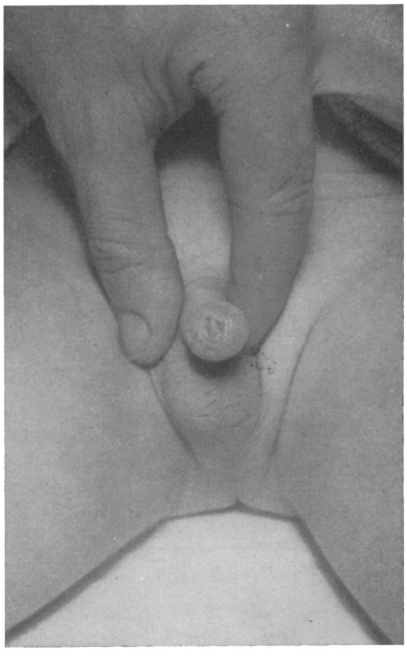

Fig. 22

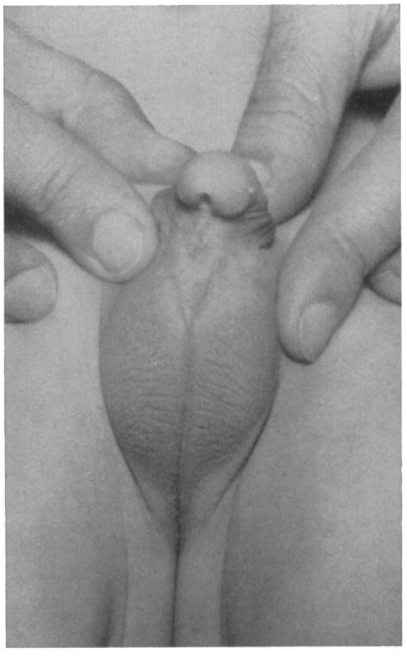

Fig. 23

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the possibility of a random event, although the latter appears rather probable. Proceeding to the findings in Case 5 we have — besides hypospadias — balanitic location of the meatus, absence of the balanopreputial groove, lateral shift of the penis. Here (for 3 symptoms) p = 2.59 per cent, thus permitting to demonstrate the existence of a hereditary etiology of this malformation, even in the absence of other genealogical data, just on the basis of a single pair.

As to case 6, with discordant hypospadias, this can be easily explained on the basis of a morbid genotype reflecting itself in only one of the twins, because they are dizygotic, i.e. with different heredity. In the absence of specific data in the genealogical tree, and the character being sex-limited, one could think, for instance, of a dominant homo- or heterozygosis in the mother and in one of the twins, or of a recessive heterozygosis in both parents, with a recessive homozygosis in only one of the twins.

In the third place we shall study an anomaly more typical to the sex, i.e. cryptorchism, which could (but not necessarily) accompany a spermatogenic defect. Its presence in pediatric age has not yet found its clinical establishment. From the phenomenological viewpoint, cryptorchism, concerning an even organ, could offer 5 possibilities of discordance, considering that the cases of mirror imaging, rather frequent in MZ twins, do not alter the concordance. These details are not always to be controlled. We therefore limit ourselves to quote data from the literature as follows: 10 MZ pairs concordant as to cryptorchism (Birkenfeld, 1929; Werner, 1929; Parhon and Simian, 1937; v. Verschuer, 1937, 2 pairs; Pfister, 1937; Greene, 1942; Glass 1946; Gedda and Rovigatti 1951; Davidson and Newberger, 1953); besides: a set of MZ triplets all three concordant as to cryptorchism (Guilleminet, Bertoye and Jacquet, 1948), 8 discordant MZ pairs (Parhon and Simian, 1937; v. Verschuer, 1937, 4 pairs; Pfister, 1937, 2 pairs; Valavoine, 1954), 1 concordant DZ pair (v. Verschuer, 1937) and 8 DZ discordant ones (v. Verschuer, 1937, 7 pairs; Turpin, Tisserand and Sans, 1940). Cryptorchism is a complex malformation, inasmuch as, far from representing a primary gene effect, it is the result of a primary effect and of many known and unknown reciprocal actions of traits in the phenotype, which may in many ways interact with the primary effect.

For example, the etiological classification of cryptorchism established by Charny and Wolgin considers as causes: deficiencies or abnormalities of the mesorchium, structural anomalies of the testis, abnormalities of the epididymis, of the cremaster muscle, of the processus vaginalis testis, of the gubernaculum, of the inguinal canal and rings, of the scrotum; hypopituitarism with secondary hypogonadism; primary hypogonadism and intersexuality.

To these causes Charny and Wolgin add a genetic or familial etiology. We believe that this item of the classification could be neglected because all the previously listed items could exist in so far as the respective genotype controlling them is mutated, without mentioning that other etiologies should be advanced as well, such as a deficiency of the corionic gonadotropin of the mother.

It is not always possible to establish what the primary effect of the gene should be,

but it is easy to realize that, whichever it may be, it must go through a mesh of epistatic conditioning of the genotypical environment and of the phenotypical conditioning, the mesh being not only very dense but also different, according to the racial, familial and individual phenotypes. Moreover the rebound a different environment could provoke for the identical trait explains that variability of expression, which we also find in MZ twins, as to cryptorchism.

On the other hand, the complexity of such a mechanism of biological automation indicates the presence of an identical genotype as the only possible justification for the identity of the finding.

We found MZ pairs as, for instance, Case 7, of 26 year-old twins concordant as to undescended left testis (Fig. 24). The first-born is single, while the second-born is married and has a child. In a set of triplets (Case 8) the two males are MZ and presented discordant cryptorchism at the age of 10 years (Fig. 25).

We shall now follow up, from the age of one year, Case 9: MZ, today eight years old twins (Figs. 26, 27, 28) who have always presented concordance in monolateral, mirror imaging cryptorchism, the first-born at left, the second-born at right. During the longitudinal study of the case we found that the second-born, who at eight months presented only one testis in the left hemiscrotum, presented two in the same hemiscrotum after the first year, one being very hypotrophic. This is a retarded descensus in an atypical place. Both had surgery for hernia and cryptorchism at the age of 3 years, and now present the post-operative sequelae in mirror imaging position.

A complex mechanism such as that of descensus testis feels, on the rebound, the exogenous factors if they act only on one of the twins, or on both but in a different degree. We know, for instance, that the conditions of the placenta could provoke a difference in nutrition towards two foetuses, as well as anoxia at birth for only one.

By means of such or equivalent mechanisms, an amplitude of oscillation is provoked in the expression of the trait which explains the finding of MZ twin pairs with discordant cryptorchism. Case 10, (Fig. 29), for instance, showed, at the age of nine years, discordant cryptorchism in the second-born, who presented inguinal retention of the right testis. We administered chorionic gonadotropin to the one with cryptorchism; at the present age of 12 years the testes in both are in the normal position.

The hereditary etiology of cryptorchism, as analyzed by the Clinical Twin Method in the above mentioned cases is confirmed by genealogical findings such as that of a sibship (Fig. 30) in which all male children, including twins, are congenitally affected with right cryptorchism (Case 11).

The preceding cases concern some relatively simple and localized malformations and show that phimosis, hypospadias and cryptorchism may represent independent hereditary units, i.e. morbid genotypes and phenotypes capable of expressing themselves according to the Mendelian pattern.

Let us now consider other cases of sex abnormalities in childhood, which express themselves not only by the localized damage we have seen, but also by generalized damage, in so far as they involve organs meant to exercise general influences, i.e. correlation systems.

Case 12 concerns a pair of 14-years-old twins (Figs. 31, 32) whose significant face traits and blood groups and subgroups are identical and stand for their MZ nature. This is also confirmed by their pathological history, both having been affected by enuresis and hernia, and both being subject to urticaria and bronchial asthma; moreover they both have difficult characters and are unfit to environmental adaptation.

Thus, we are amazed to find a difference between them of nearly 5 cms. in height and 1,500 gms. in weight. An examination of the genital organs shows, in the first-born, a curved penis and both testes in the correct place (Fig. 33); in the second-born the penis is more curved and the urinary meatus is artificial, following corrective surgery for hypospadias, at the middle third of the penis (Fig. 34); the testes are not in place and can be found in the inguinal canal, the right one being higher. Skull X-rays show a hypoplastic sella turcica, more remarkable in the second-born (Figs. 35, 36). The karyotype is normal (Figs. 37, 38). From the psychological view-point, sex interest is present in the first- and absent in the second-born. Sex chromatin analysis shows male characteristics in both. The urinary-17-ketosteroids are 7.8 and 5.3, and the gonadotropin excretion 3.5 and 3.2 u. p., in the first- and in the second-born, respectively, over 24 hours.

Clinical comparison of the twins permits individualization of two « minus-variants » in the second-born. On the one hand, his auxological and psychosexual development is deficient; on the other, he has hypospadias, cryptorchism and a reduced value, both absolute and relative, of the urinary-17-ketosteroids. Such a finding is only possible by means of the twin method, because, if the second-born were a sibling, we would not have a term of isogenic comparison for exactly establishing his lower development in height, weight and psychological status. As to the *primum movens* of the above discordances, we may believe it to be a global hypophyseal deficit due to a difficult delivery, the pregnancy having ended at 6 months and a half, on account of abruption of the placenta.

Six years ago, we examined and reported these 14-year-old undoubtedly MZ twins (Case 13), who weighed respectively 67 and 66.5 Kgs., both showing abundant panniculus adiposus with a pseudo-female distribution in correspondence to the pubis and the mammary region, an accumulation in the lumbar region, and also with a female distribution of hair (Figs. 39, 40). In both, the genital apparatus showed a marked hypotrophy of the penis, scrotum and testes, the latter having been found in place but moving towards the inguinal canal (Figs. 41, 42). The genital hypotrophy is remarkable, but less so in the second-born. The anamnesis revealed that the gain in weight began at the same time in both, at the age of 7 years, without any modification of hunger, thirst and of the asleep/awake rhythm; the basic metabolic rate was —2 per cent in the first- and —8 per cent in the second-born. Skull X-rays showed in both the sella turcica covered by an osteofibrotic bridge and also a hypertrophic lamina quadrilatera. We diagnosed an adiposogenital degeneration, which is also proved by the presence of reddish stripes at the gluteal regions and by the impossibility of a dosage of the urinary gonadotropin in both. Moreover, they presented features of cortical hyperadrenalism, as shown

CASE 7

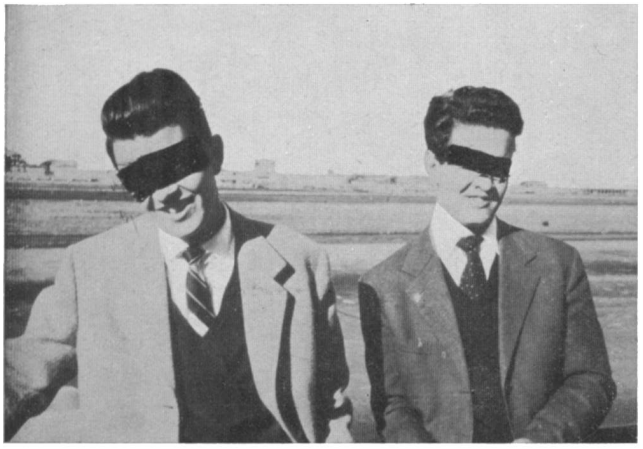

Fig. 24

CASE 8

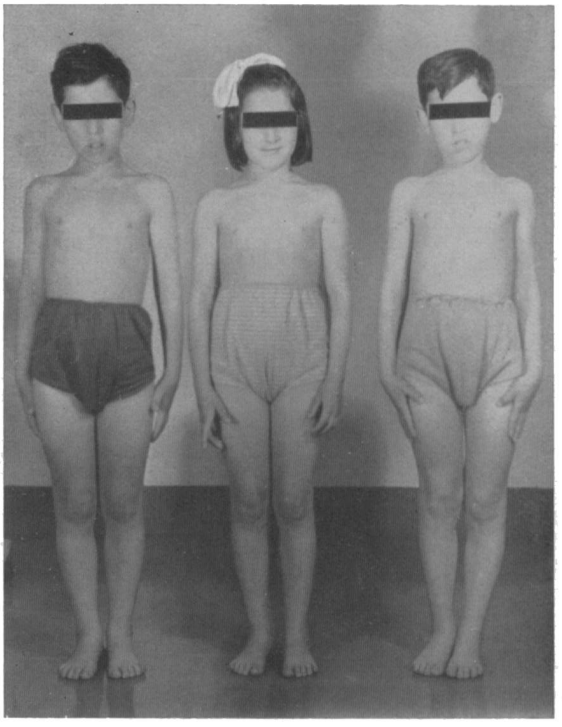

Fig. 25

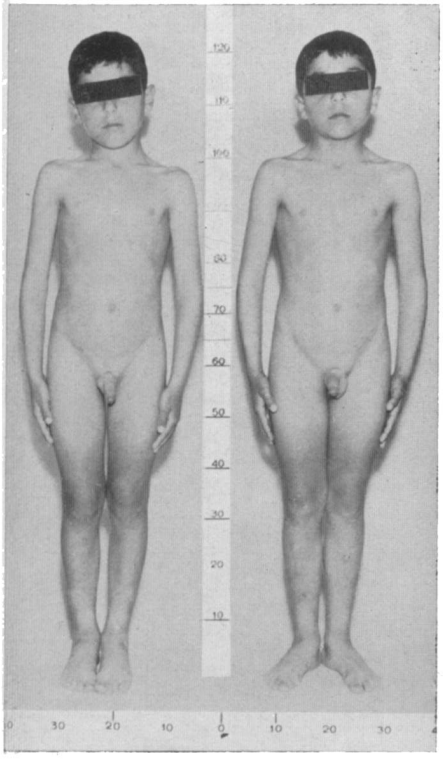

Fig. 26

CASE 9

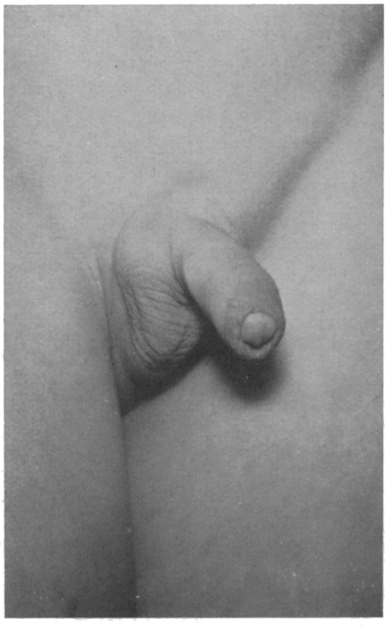

Fig. 27

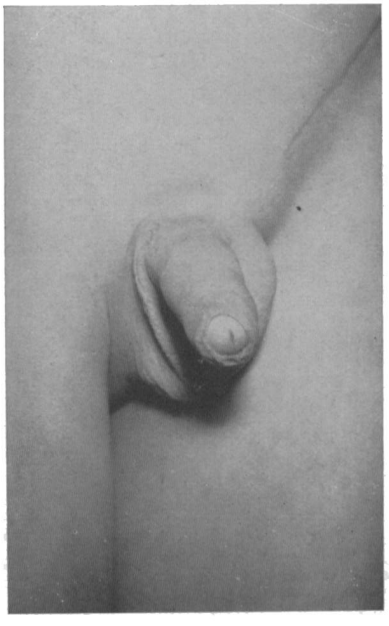

Fig. 28

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CASE 10

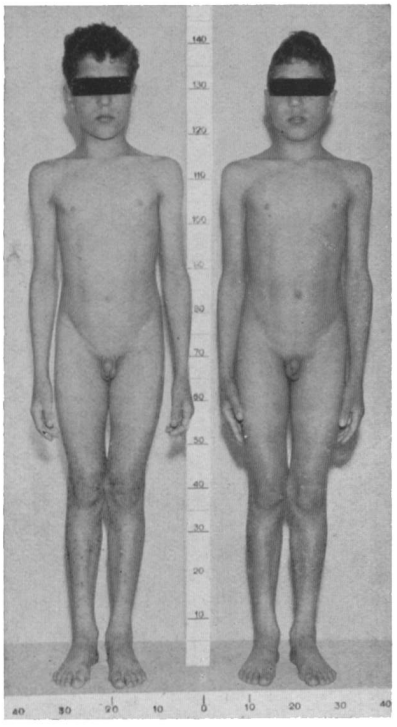


Fig. 29

CASE 11

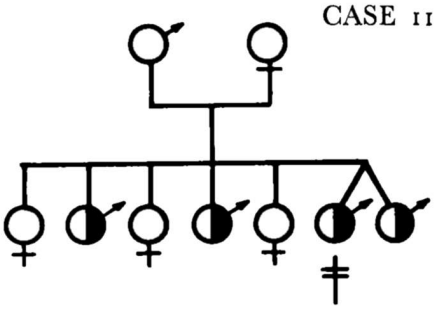
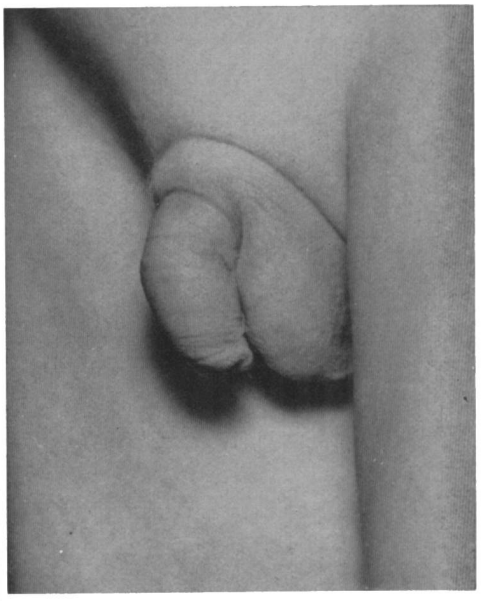


Fig. 30

CRYPTORCHISM

Fig. 33



CASE 12

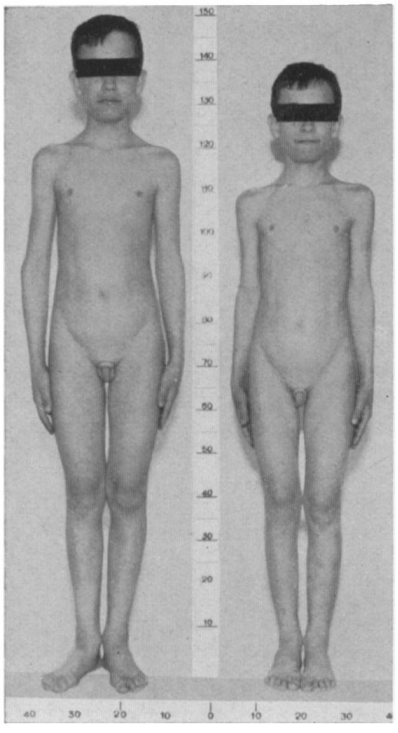


Fig. 31

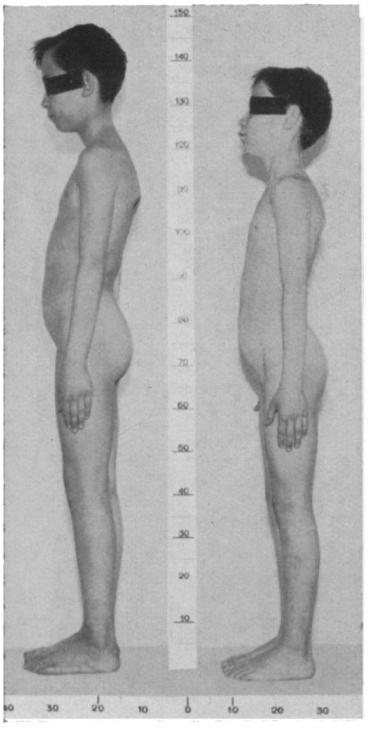


Fig. 32

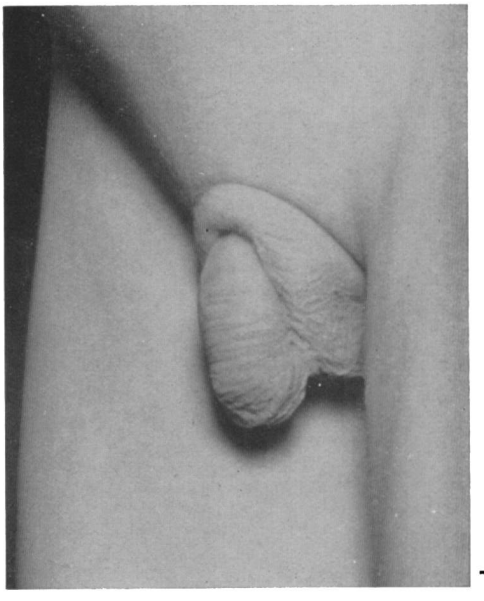


Fig. 34

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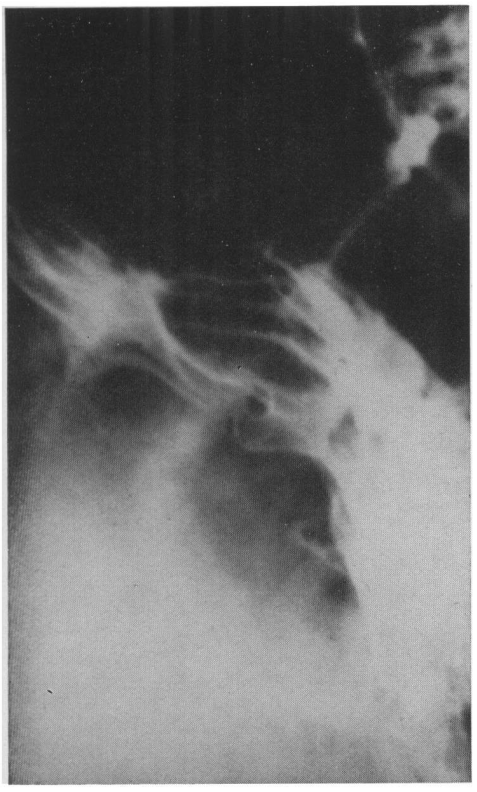

Fig. 35

Fig. 36

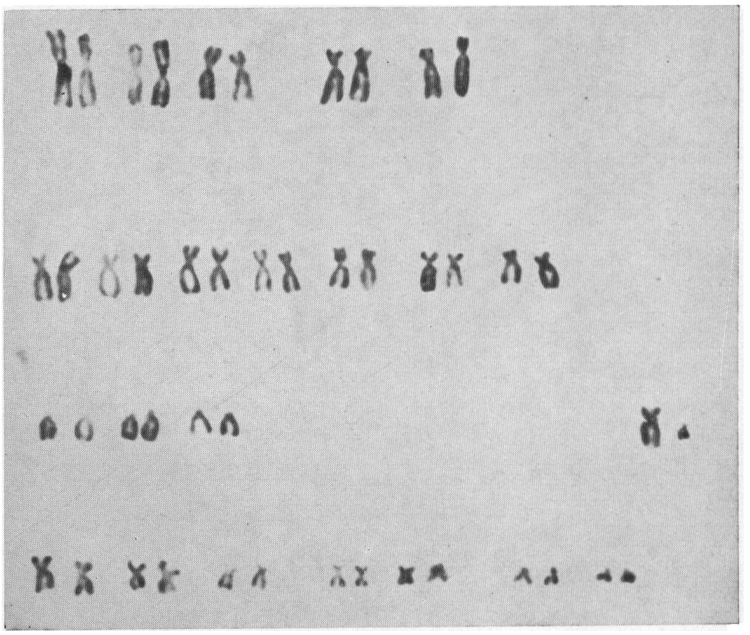

Fig. 37

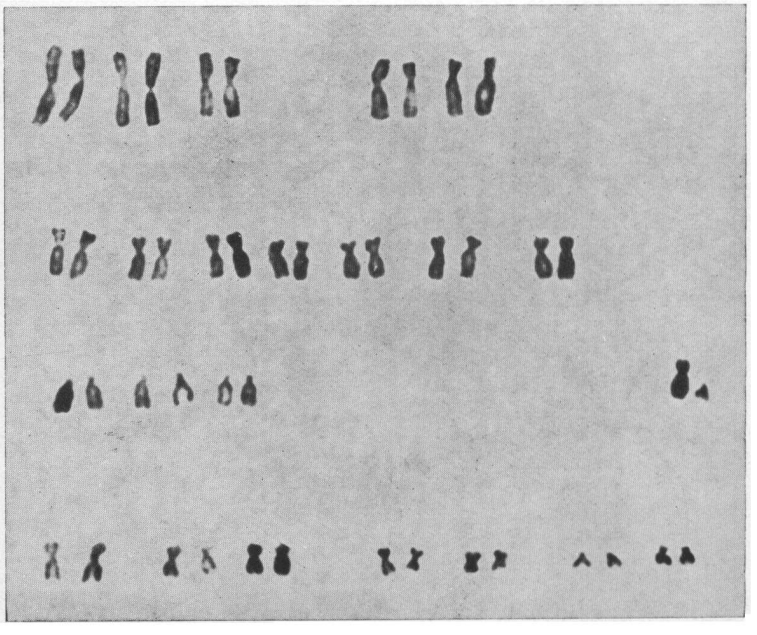

Fig. 38

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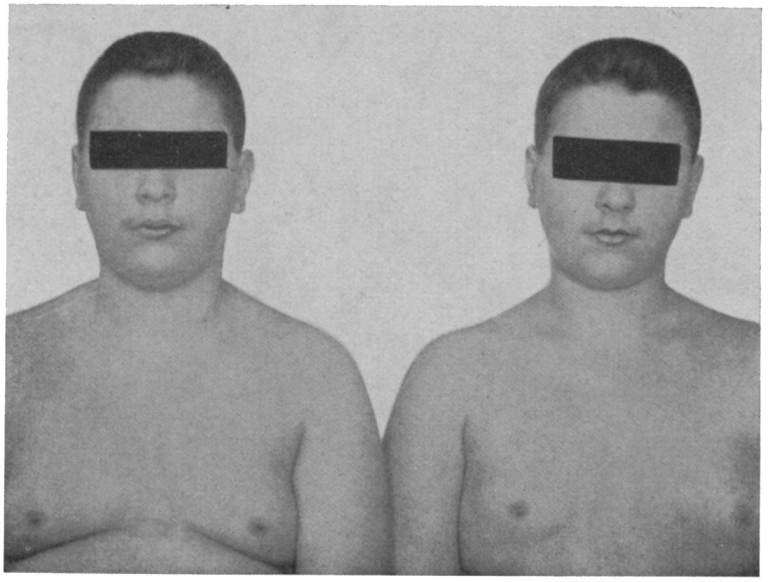

Fig. 39

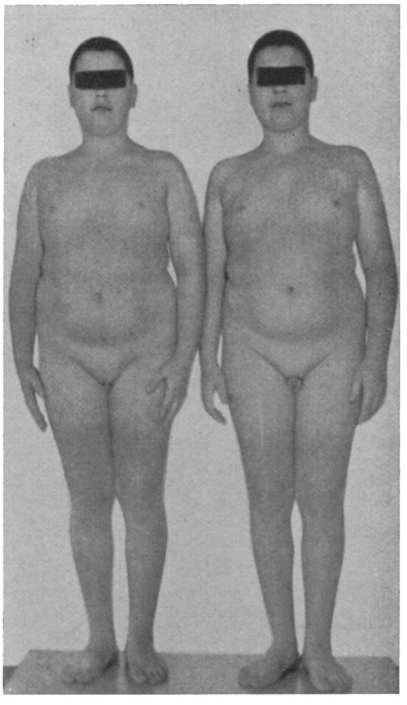

Fig. 40

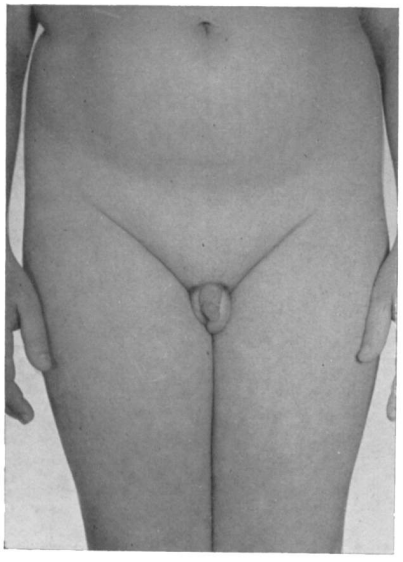

Fig. 41

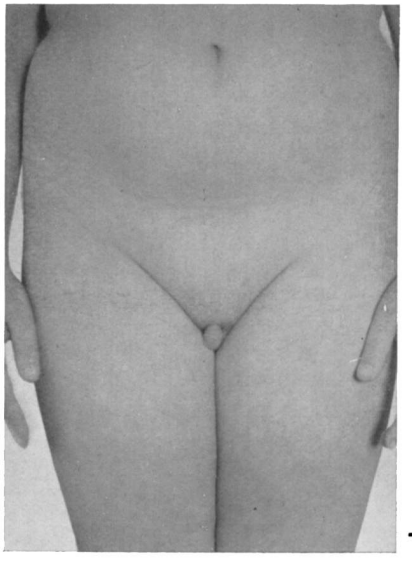

Fig. 42

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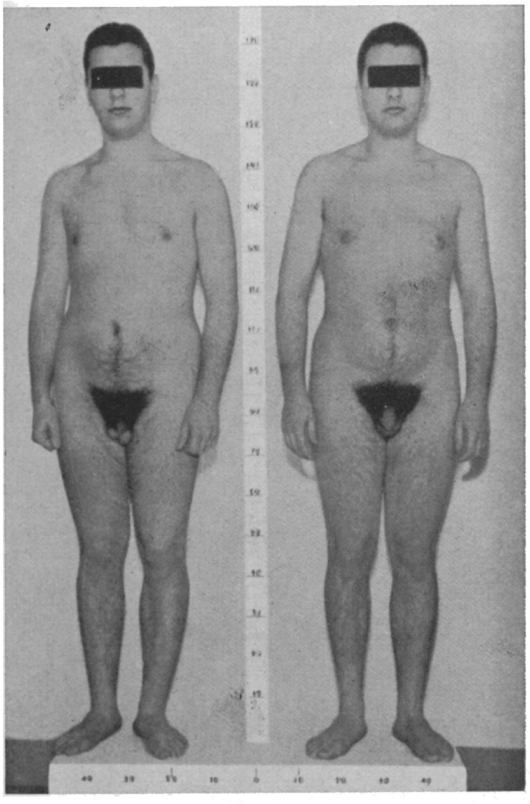

Fig. 43

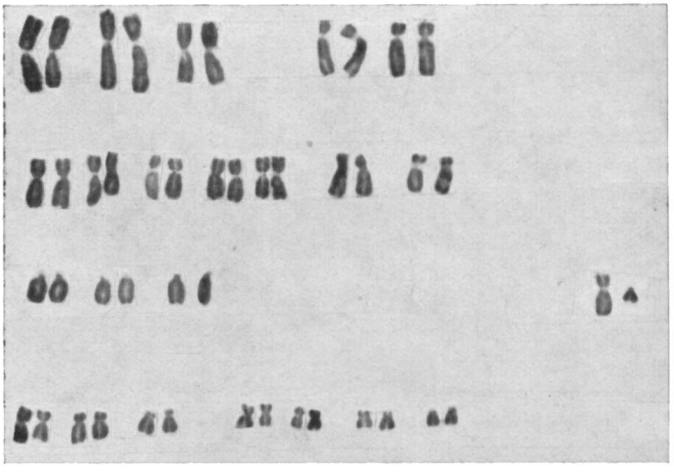

Fig. 44

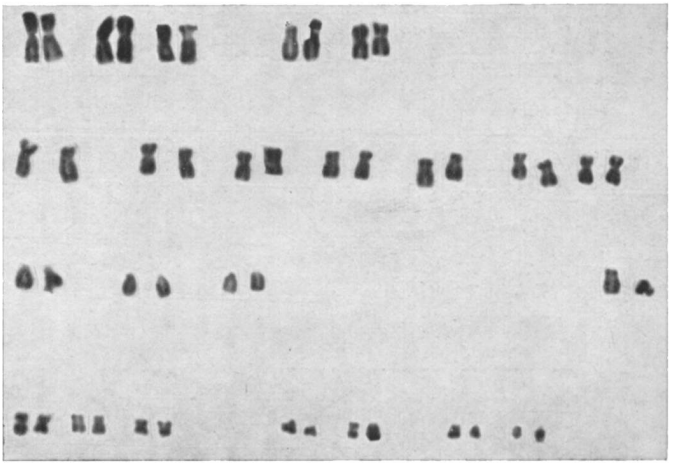

Fig. 45

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by hyperglycemia (I = 1.75; II = 1.60), by a relative increase of the urinary 17-ketosteroids (I = 12.35 mgs.; II = 8.85 mgs. over 24 hours), and by relative hypertension (I = 145/90; II = 125/80). And here we have the present situation, at 18 years of age (Fig. 43). The twins weigh respectively 85.000 and 83.100 Kgs. and show the following findings: glycemia: I = 1.00 per cent, II = 1.10 per cent; urinary 17-ketosteroids: I = 7.8 mgs., II = 7.2 per cent; urinary gonadotropin: I = 8.02, II = 7.00. The karyotype is normal in both (Figs. 44, 45).

The duplication of the syndrome and its regression shows the genotypical determination and control of the hormonal cadence, also in abnormality. These cadences are caused by what Gedda terms the « chronaxy » of the gene. Only one of the twins underwent consistent gonadotropin therapy, while both were treated with testosterone. But it may also be that the twins presented an identical favourable evolution of the syndrome due to their genotype-controlled hormonal cadence. Should the result be the effect of testosterone, it would prove a hereditary concordant sensitivity to hormonal treatment; and this, again, could be referred to the new field of pharmacogenetics.

Case 14, MZ, 9-year-old, have come to the Mendel Institute with a concordant anamnesis of bronchitis, tonsillitis and otitis. A slight difference in height and weight, from birth up to now, is recorded, as well as a difference in school performance, which is poor in the first- and excellent in the second-born. An unusual confirmation of monozygosity is provided by a concordant sinusal arrhythmia of the respiratory type and vertical heart position. Both are also heavy eaters. General examination shows diffuse adiposis with female-like distribution (Fig. 46). As to external genitalia (Figs. 47, 48), deficient development of the penis and scrotum and bilateral cryptorchism is observed in both. In the first-born, the testes are not palpable and are probably in an endoabdominal position, while in the second-born they are found in the inguinal canal. On the basis of the objective findings and the urinary 17-ketosteroids dosage (I: 2.77 mgs.; II: 2.55 mgs. over 24 hours) and of the gonadotropin excretion (I: 5.37 u. p.; II: 5.55 u. p. over 24 hours) an adiposogenital dystrophy was diagnosed. The karyotype is normal.

The « primum movens » of the adiposogenital dystrophy in this pair could be referred to the genotype controlling the diencephalo-hypophyseal system with a quantitative hypogonadal effect (defective development of the external genitalia, hyponormal urinary 17-ketosteroids elimination, abnormal gene-chronaxy, missing testium descensus) and negative general effect (adiposity and feminization). The Clinical Twin Method proves that the whole picture has a hereditary etiology. A further proof is given by the genealogical tree (Fig. 49), where we find three cases of cryptorchism in three paternal first cousins and another case in a maternal cousin; the latter and another maternal cousin presented obesity during infancy and puberty.

Finally, we have Case 15, a pair of male twins who came to the Mendel Institute at the age of nine years (Fig. 50), exceeding the average values for their age concerning weight (I+20, and II+22 Kgs.) and height (I+3 and II+3.5 cms.). Obesity began at the age of about 6 years, together with the appearance of polyphagia and

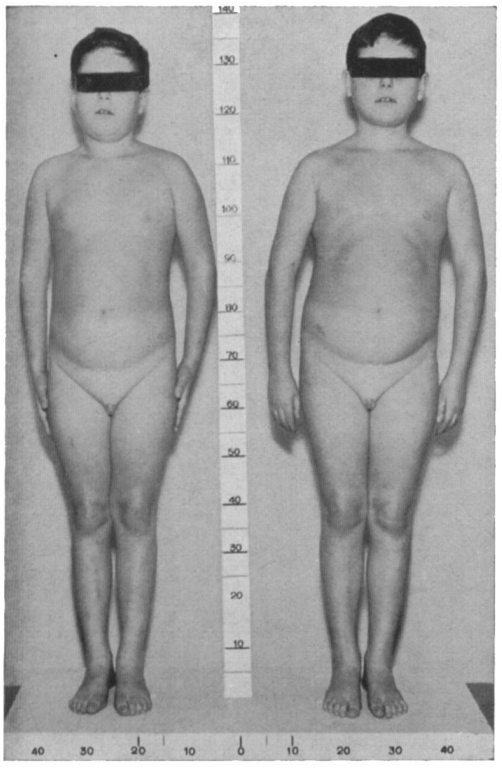

Fig. 46

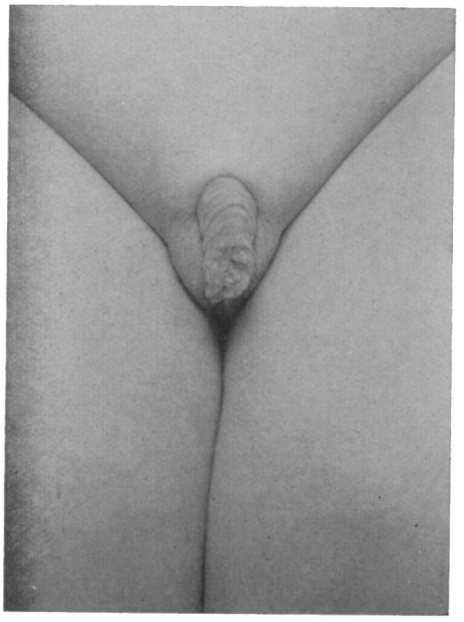

Fig. 47

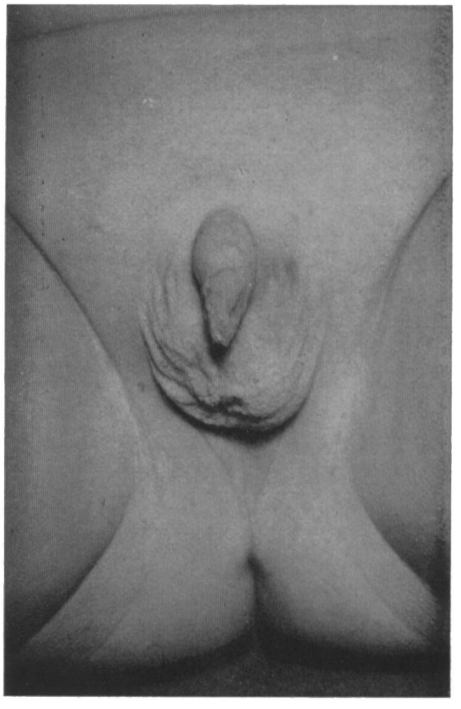

Fig. 48

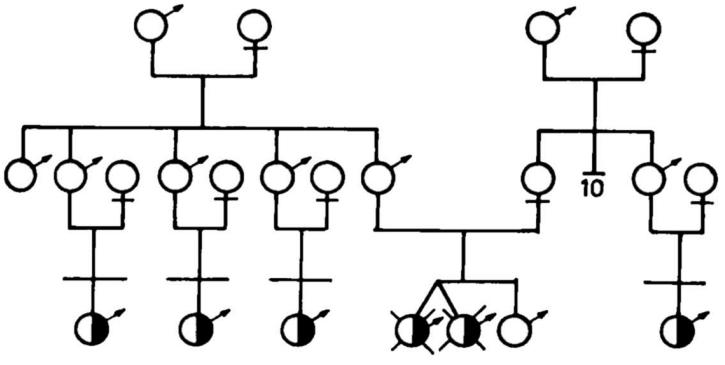

Fig. 49

polydipsia. The panniculus adiposus is remarkable in both, especially at the neck, at the mammary region (gynecomastia) and at the flanks. Local examination showed hypoplastic penis (as in a 3-year-old boy) and hypotrophic testes (Fig. 51). The twins show differences in the ABO and Rh-Hr blood group systems (I = A_1 MN Rh_z Rh_1; II: B MN Rh_2 Rh_2); they also present nystagmus in the lateral eye movements, hypermetropia, bilateral blepharoconjunctivitis. Besides, they have hypoglycemia (I = 0.85; II = 0.78 mgr. $^0/_{00}$), diminished urinary 17-ketosteroids in both (about 2 mgr. over 24 hours) and syndactily between the second and the third toes bilaterally. The basal metabolic rate amounts to +4% in the first and +8% in the second-born. The arterial pressure is 120/90 in both.

The different heredity of the twins, which is hidden to such a degree by the concordant general proportions of the body and by the morbid picture, is indicated the blood groups and by skull X-rays, insofar as the sella turcica is normal in the first-born, but very small, closed above and with a slanting major axis in the second-born. Also from the mental point of view, we see a diversity of intelligence and emotivity, remarkably higher in the first-born. Re-examined at the age of 13 years (Fig. 52) the twins present a worsening of the morbid picture. Examination of the genitalia has shown the testes to be in the correct place in both, but of reduced volume; and the penis hypoplastic in the first- (Fig. 53) and still more so in the second-born (Fig. 54). In the genealogical tree we have found cases of obesity, syndactily and mental diseases (Fig. 55). We made a diagnosis of Laurence-Moon-Bardet-Biedl syndrome. In fact, among the fundamental symptoms, the hypogenitalism quoted by Laurence and Moon (correspondent to Bardet-Biedl's hypophyseal obesity) exists in our twins in the form of obesity with hypogenitalism, which, however, could derive not only from hypophyseal, but also from diencephalic damage denounced by polyphagia and polydipsia. Polydactily (Laurence and Moon) or syndactily (Bardet and Biedl), as in our specific case, is present in both. The oligophrenia stressed by Biedl is present especially in one twin, but also in the other a deficient I. Q. is developing. The tapetoretinal damage is absent, although other traits of the ocular pathology are present. We should remember, however, that, according to Schachter, retinitis pigmentosa is present only in 82 per cent of the cases. The study by the Clinical Twin Method is deemed interesting because, as the concordance of the syndrome is certain, we can evaluate the relative importance of given symptoms, such as oligophrenia, and discriminate the pathogenesis, as we have done in the discussion between diencephalic and hypophyseal mechanism.

In remembering a case of MZ twins, both affected by the Laurence syndrome, described by Moench (1954), we deem our case in concordant DZ twins to be equally important, because it proves the high penetrance of the genotype which imposes itself in spite of the relatively different heredity of the two partners.

Concluding, we express the hope of having made ourselves sufficiently understood, notwithstanding the limited time, which prevented us from advancing many other considerations concerning our cases.

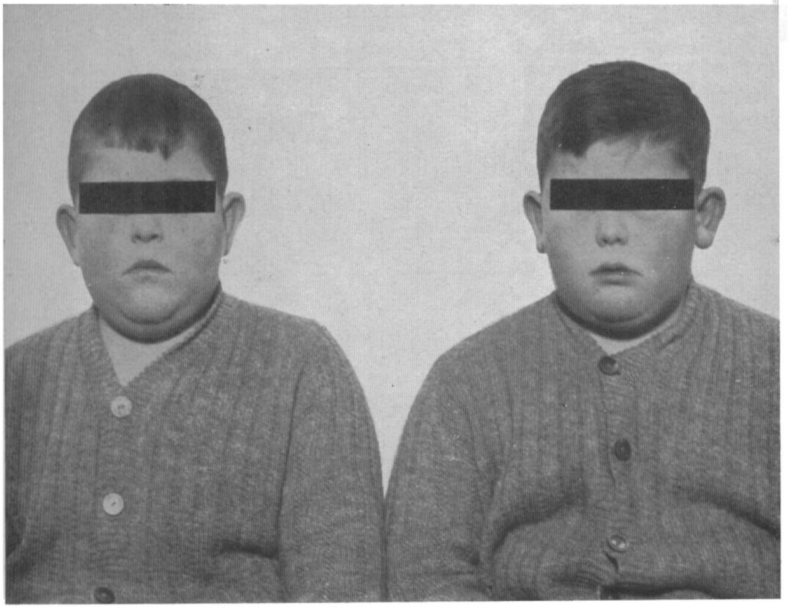

Fig. 50

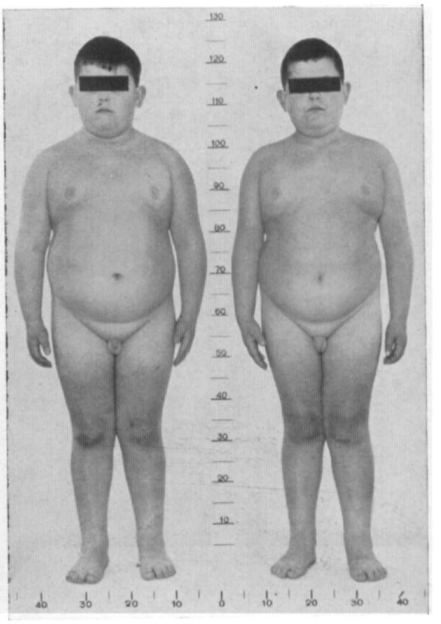

Fig. 51

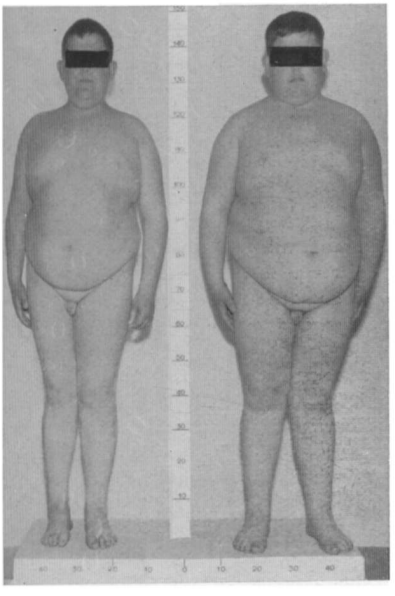

Fig. 52

Fig. 53

Fig. 54

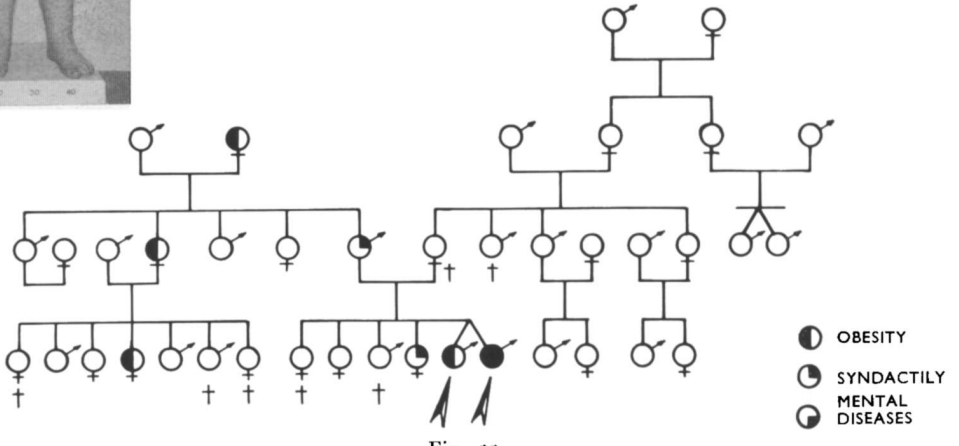

Fig. 55

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Summary

First of all the Authors stress the importance of twin studies as a method of analysis of the pathological phenomena from a hereditary standpoint: to this aim, the Interzygotic Twin Method may be used in statistical studies, and the Clinical Twin Method in clinical ones. On this basis, the Authors report their observations, on a remarkable number of male twin pairs, affected by anomalies or syndromes including one or more genital dysfunctions, either in infancy or adolescence. Numerous cases of phimosis are thus presented, where the higher concordance in pairs of MZ twins stands for a hereditary conditioning; cases of hypospadias, showing a perfect symmetry of the malformation in the cotwins; cryptorchism, with various possibilities of presentation of the anomaly in the intrageminal comparison. The Authors also describe in detail, making an analytical intra-pair comparison of the symptoms and laboratory data, some cases of complex adiposogenital dystrophy, as well as one case of Laurence-Moon-Bardet-Biedl syndrome with different clinical manifestation in a DZ pair. The longitudinal study carried out over many years on some of the pairs affected by the above mentioned clinical pictures, and the clinico-statistical analysis of the cases under consideration allow the Authors to draw a number of positive conclusions concerning the variable, genotypic conditioning of the sex anomalies considered: in this field, as well as in many others of nosography, the Clinical Twin Method appears to be highly useful in practice, and unique by reason of its peculiarity.

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RIASSUNTO

Gli AA. ricordano anzitutto l'utilità dello studio dei gemelli come metodo di analisi dei fenomeni patologici da un punto di vista ereditario: a questo scopo si può utilizzare o il metodo gemellare interzigotico, in sede statistica, o il metodo clinico gemellare, in sede clinica. Su questa base vengono riferite le osservazioni condotte su un considerevole numero di coppie gemellari maschili, affette da anomalie o da sindromi includenti una o più disfunzioni genitali, nell'infanzia o nell'adolescenza.

Vengono così presentati numerosi casi di fimosi, in cui la maggiore concordanza in coppie di gemelli MZ depone per una influenza ereditaria; di ipospadia, con l'evidenza di perfetta simmetria della malformazione nei due cogemelli; di criptorchidismo, con varie possibilità di presentazione del difetto nel raffronto intrageminale. Vengono infine descritti in dettaglio, con paragone analitico intracoppia dei sintomi e dei dati di laboratorio, alcuni casi di sindromi complesse adiposo-genitali ed un caso di sindrome di Laurence-Moon-Biedl, con diversa espressività clinica in coppia DZ.

Lo studio longitudinale condotto per anni in alcune delle coppie affette dai quadri suddetti e l'analisi clinico-statistica della casistica studiata permettono di giungere a conclusioni positive circa il condizionamento genotipico, in grado variabile, delle anomalie sessuali prese in considerazione. In questo campo, come in molti altri della nosografia, l'adozione del metodo clinico-gemellare appare pertanto di grande utilità pratica e, per la sua peculiarità, insostituibile.

RÉSUMÉ

Tout d'abord les Auteurs rappellent l'importance de l'étude des jumeaux en tant que méthode d'analyse des phénomènes pathologiques au point de vue de l'hérédité; dans ce but, dans les études statistiques l'on peut utiliser la méthode jumelaire intra-zygotique, et dans les études cliniques la méthode jumelaire clinique. C'est sur cette base que les Auteurs rapportent les observations conduites sur un nombre considérable de couples de jumeaux de sexe masculin atteints d'anomalies ou syndromes comprenant une ou plusieurs anomalies génitales chez l'enfance ou l'adolescence. Les Auteurs présentent aussi de nombreux cas de phimosis, où la plus haute concordance chez les couples MZ indique un conditionnement héréditaire; d'hypospadie, avec des preuves d'une parfaite symétrie de la malformation chez les deux partenaires; de cryptorchidie, avec différentes possibilités de présentation du défaut au sein de la comparaison intragéminale. Les Auteurs décrivent enfin, en détail, avec comparaison analytique intra-couple des symptômes et des données de laboratoire, quelques cas de syndrome adiposo-génital, ainsi qu'un cas de syndrome de Laurence-Moon-Biedl, avec différente expressivité clinique chez un couple DZ. L'étude longitudinale conduite pendant des années chez quelques-unes des couples atteintes par les tableaux susdits et l'analyse clinique-statistique des cas étudiés permettent d'atteindre des conclusions positives concernant un conditionnement génotypique, de dégré variable, des anomalies sexuelles considérées. Dans ce secteur, ainsi que dans beaucoup d'autres de la nosographie, l'adoption de la méthode jumelaire clinique semble être très utile au point de vue pratique, et unique en raison de ses caractéristiques spéciales.

ZUSAMMENFASSUNG

Verf. betonen vor allem die Nützlichkeit der Zwillingsforschung als analytische Methode zur Untersuchung der krankhaften Veränderungen auf ihre Erbbedingtheit: man kann dabei entweder die interzygote Zwillingsmethode für statistische Zwecke oder die klinische Zwillingsmethode im klinischen Praktik anwenden. Dementsprechend wird über Beobachtungen berichtet, die an einer beträchtlichen Anzahl männlicher Zwillingspaare angestellt wurden, die im Kindes- und Jugendlichenalter Anomalien oder Syndrome mit einer oder mehreren Geschlechtsdysfunktionen aufwiesen.

Vorgetragen werden: zahlreiche Fälle von Phimose, bei denen die größere Konkordanz der EZ-Paare für einen Erbeinfluß spricht; von Hypospadie, wo die Mißbildung bei beiden Paarlingen völlig symmetrisch war; von Kryptorchismus, wo ein intrageminaler Vergleich verschiedene Möglichkeiten ergab. Ausführlich behandelt mit analytischen Vergleich den Symptome und der Labor-befunde zwischen den Paarlingen wurden einige Fälle von komplexe adiposogenitalen Syndromen, sowie ein Fall von Syndrom nach Laurence-Moon-Biedl mit verschiedener Ausdrucksform in einem ZZ-Paar.

Einige Zwillingspaare mit obiegen Krankheitsbildern wurden Jahre hindurch beobachtet; der diesbezügliche Längsdurchschnitt und die klinisch-statistische Analyse der untersuchten Kasuistik gestatten es, die Erbbedingtheit in verschiedenem Grade der zur Frage stehenden Geschlechtsanomalien positiv anzusehen. Wie auf anderen Gebieten der Nosographie erscheint auch hier die Anwendung der klinischen Zwillingsmethode äußerst nützlich und in ihrer Art unersetzlich.

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