The Management of Paediatric Hermaphroditism

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SUMMARY

The management, between 1963 and 1973, of 33 cases of hermaphroditism in infants and children at the Red Cross War Memorial Children's Hospital, Cape Town, is presented. The authors favour a simple classification. There were 8 cases of female pseudohermaphroditism, 6 cases of testicular feminising syndrome and 19 cases of hermaphroditism. Of the latter, 13 were true hermaphrodites, 3 mixed gonadal dysgenesis and 3 male pseudohermaphrodites. Tables presenting the external and internal morphology, gonadal identity and illustrations of these, are presented. Results of leucocyte and tissue chromosome cultures are shown.

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Hermaphroditism is a rare occurrence and most doctors will not be consulted on a case during their professional lives. This is particularly true in respect of hermaphroditism recognised in the neonate, since it is commoner in the Black population and such infants are more often delivered by midwives in the homelands.

Fortunately, the homespun wisdom of medically unsophisticated people confronted with the problem of a newborn hermaphrodite usually guides them to assign the baby to the sex it most closely resembles in its external genital appearance, and this, in essence, is what has proved to be the best for the child in the majority of cases. In our experience at the Red Cross Children's Hospital we have seldom had to reassign such a child to a sex contrary to the one initially chosen by the parents. We have, however, more than once had to reassign infants delivered by doctors. This is because the medical attendant, confronted with the problem of a newborn infant of doubtful sex, is more than likely to consult an individual specialist, and no individual — endocrinologist, geneticist, paediatrician, gynaecologist, urologist or plastic surgeon — is adequately equipped to investigate and make the all-important decision alone.

Mistakes are made time and again. One of us recently spent a month at Johns Hopkins Hospital, Baltimore, USA, which is considered to have outstanding experience in this field, and was heartened to find, in working through their records of the past 35 years, that the staff there have similar problems, correcting mistakes made by individual consultants dealing with such cases outside the hospital. It confirmed the conviction that a modern children's hospital with a fully diversified team experienced in dealing with hermaphroditism in infants, is the institution best equipped to investigate, diagnose and manage these children.

It is essential to realise that, unlike hermaphrodites presenting themselves for treatment for the first time in adulthood, these infant hermaphrodites have a very good chance of a well-adjusted adult sex life, provided they are assigned to the sex best suited to what they have available in genital equipment, even if this is contrary to their genetic or gonadal identity, and that they are then steadfastly reared in the chosen gender and the necessary corrections made as early as possible, so that neither they nor their parents shall have any doubt as to their sex.

The reasons for the mistakes lie with the confusion engendered by intricate classifications and terms such as male and female intersex and male and female pseudohermaphrodite; and by over-rating the importance of chromosomal and gonadal identity. These are the pitfalls that lead the occasional consultant, enthusiastic about dealing with such a case, to assign a sex often quite unsuited to the available genital equipment. Male pseudohermaphroditism is a particularly bad term, and the findings of male chromatin pattern, male karyotype and testes, are notorious for misleading the inexperienced into assigning the male sex to infants with hopelessly inadequate male equipment. The margin of error is minimised by employing a fully representative team, and a simple classification.

The Representative Team

The team at the Red Cross War Memorial Children's Hospital consists of the following: gynaecologist (director), urologist, plastic surgeon, child psychologist, radiologist, endocrinologist, geneticist and histologist.

The former four clinical members are best qualified to make the all-important decision as to sex assignment, since they have the experience to know what end-result can be achieved anatomically, functionally and psychologically. The other members have an equally vital role in helping them to reach this decision, and in making the ultimate diagnosis.

Classification Used

We found the following simple classification a safe and workable one, and one which should reduce the risk of error inherent in nomenclature to a minimum:

(1) female pseudohermaphroditism; (2) testicular feminising (androgen insensitivity) syndrome; (3) hermaphroditism.

Female pseudohermaphroditism. This can be (*a*) due to adrenal hyperplasia (which can be confirmed or excluded

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unequivocally by laboratory investigation); (*b*) due to administration of a masculinising progestogen to the mother during pregnancy or (*c*) idiopathic. The latter, when detected in infancy, carries an excellent prognosis for correction to adequate females who will present few problems in rearing and will be potentially fertile adults.

Female pseudohermaphroditism is therefore a safe nomenclature.

The testicular feminising syndrome is another clear-cut entity, easily diagnosed where testes are palpable in the inguinal or labial situations in children with completely or almost completely feminine external genitalia, but no vagina or only a rudimentary vagina and no uterus. It is confirmed by male chromatin and karyotype patterns. The diagnosis is often missed if a slightly prominent clitoris does not draw attention to possible ambiguity. It is not infrequently made only when a testis is found in a hernial sac in someone reared as female — as all these should be.

Again the nomenclature is safe. It is only when such children are classified as male pseudohermaphrodites that there is a risk of erroneous assignment — to reiterate, this is a bad term serving no purpose other than, by inference, misleading the inexperienced into assigning the male sex to an hermaphrodite infant with testes, regardless of the equipment available for adult sex life as a male.

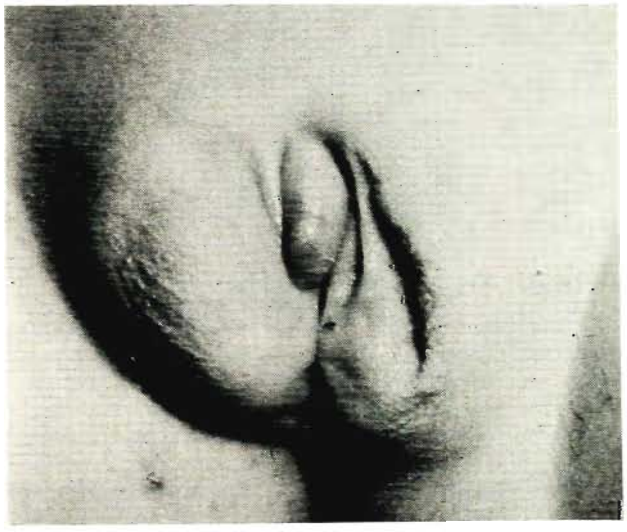

Fig. 1. Originally assigned as a male on the basis of male genotype (sex chromatin and karyotype). Totally inadequate male genitalia.

Fig. 1 illustrates a typical case where the male sex had been assigned on the strength of male buccal smears, karyotype, and palpable testes, and as can be seen, there is no hope of giving this child an adequate phallus. We feel the term male pseudohermaphroditism should be discarded, and that all intersex infants, excluding groups 1 and 2, should be termed simply hermaphrodites.

Hermaphroditism at least implies, correctly, that there is a choice to be made, and this choice is one of sex assignment and is all-important. The final accurate diagnosis (i.e. whether the child is a true hermaphrodite, male pseudohermaphrodite, or has mixed gonadal dysgenesis, etc.) is of academic importance and is only made on gonadal histology, which could be well after the gender of rearing has been decided and implemented.

PATIENTS

The series upon which this article is based consists of 33 patients seen and managed by one of us (J.P.R.) over approximately the past 10 years, and has not been published before. Cases 6, 8, 11, 12, 19, 27, 28 and 30 have been seen in consultation and managed at Groote Schuur Hospital, Cape Town, and Edendale Hospital, Pietermaritzburg, and in private practice. The remainder have all been under our joint care at the Red Cross Children's Hospital.

These 33 cases were classified as follows:

Female pseudohermaphroditism. There was a total of 8 patients—5 congenital adrenal hyperplasia, 1 maternal progestin therapy and 2 idiopathic.

Testicular feminising (androgen insensitivity) syndrome. There were 6 patients—3 with completely feminine external genitalia, and 3 with slightly enlarged clitoris. (Two of the latter were cousins — born to identical twin sisters.)

Hermaphroditism. There were 19 patients, of whom 13 were classed as true hermaphrodites—7 were reared as females and 6 as males. Three had mixed gonadal dysgenesis — 1 was reared as a female and 2 as males. Three were classed as male pseudohermaphrodites — 1 was reared as a female and 2 as males.

INVESTIGATION OF CASES

Our patients are investigated as follows: familial history is examined with regard to adrenal hyperplasia and testicular feminisation, and whether the child's mother received progestin therapy during pregnancy.

External genitalia, including phallus, vestibule and urethra are investigated, and the child is examined for labioscrotal or inguinal swellings and inguinal hernia, and rectal palpation for uterus is done.

Special Investigations

These include estimation of 17-ketosteroids, total oxogenic steroids and pregnanediol in a 24-hour specimen of urine, and the dexamethasone suppression test, which is essential to confirm or exclude adrenal hyperplasia, and which should be done as soon as possible, as the salt-losing variety can be fatal.

Buccal smears are taken.

Chromosome culture and karyotyping of the infant's blood are done, which will confirm the testicular feminising syndrome if the results demonstrate a child with female external genitalia to be genetically male (buccal chromatin negative and XY sex chromosomes). Female pseudohermaphrodites and most true hermaphrodites have positive buccal smears and XX sex chromosomes.

Genitography

Genitography is especially useful for showing how much, if any, vagina is available. This is of considerable value in

hermaphrodites, where there is a choice of assigning either the female or male sex—if there is an adequate vagina, surgical correction to the female sex is much easier. We used to combine genitography with endoscopy under anaesthesia in the operating theatre, but we have lately preferred to have this investigation done without anaesthesia by our senior radiologist[1] in his department, where facilities for positioning and teleradiographic screening combined with technical skill have produced far more informative pictures (Figs 2 and 3).

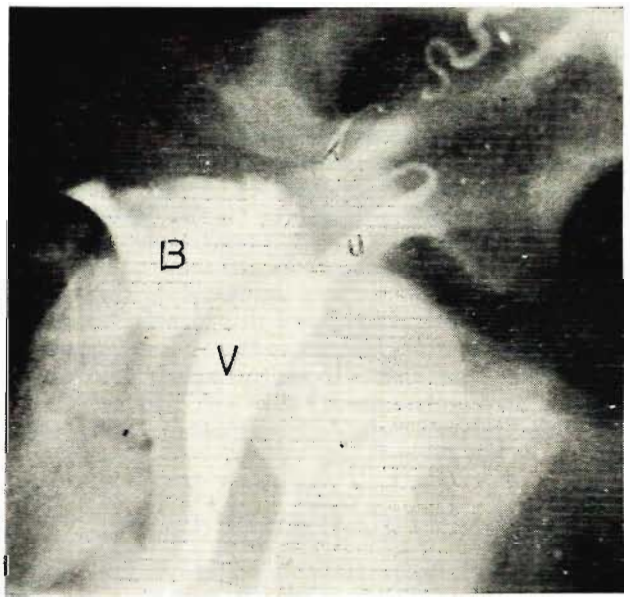

Fig. 2. Case 19. Genitography outlining the bladder and genitalia. B = bladder; V = vagina; U = unicornuate uterus; T = unilateral Fallopian tube.

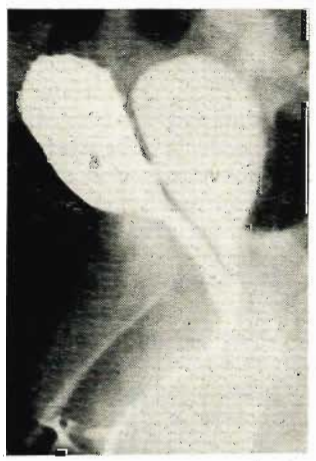

Fig. 3. Case 20. Vaginal size easily demonstrated by genitography. Note very small communication with urogenital sinus, and single external opening.

Examination under anaesthesia and endoscopy are carried out by the urologist and gynaecologist together. In cases of female pseudohermaphroditism, endoscopy will usually reveal a common urogenital sinus with separate urethral and vaginal orifices opening off it, 1 - 2 cm deep to a single vestibular aperture. In these cases and in some cases of true hermaphroditism the vaginal opening may be very small and inadequate for the panendoscope to be passed. It is here that genitography can be of particular value in determining whether the vagina is rudimentary or of adequate size (Fig. 2). More commonly, the endoscope can be passed with ease into both orifices, and if so, a cervix can usually be seen at the vaginal vault.

SEX ASSIGNMENT AND DIAGNOSIS

Female Pseudohermaphrodites

Eight patients were found to be female pseudohermaphrodites (Table I). In 5 patients, steroid values confirmed congenital adrenal hyperplasia. One mother had had prolonged therapy for habitual abortion with nor-ethisterone during pregnancy. The 7th patient had the typical external genitalia and urogenital sinus of a female pseudohermaphrodite, but as neither of the above-mentioned two aetiological factors applied, diagnosis had to be confirmed by exploratory operation and gonadal biopsy, which revealed a normal uterus and ovaries. She is, therefore, an idiopathic female pseudohermaphrodite.

The 8th patient was the only one of this group who had separate urethral and vaginal openings in the vestibule. She had quite a large phallus and was thought in all probability to be a true hermaphrodite, but exploration revealed normal ovaries, uterus and tubes.

These 8 children were all designated and reared as females from infancy.

Testicular Feminising Syndrome

Six children were classed as having testicular feminising syndrome (Table II). Three were diagnosed upon discovery of testes in hernial sacs in children reared as girls. One was diagnosed after routine investigation on account of ambiguous genitalia at birth. The remaining 2 were cousins born to identical twin sisters, investigated elsewhere shortly after birth for ambiguous genital appearance, and designated male on the strength of male buccal chromatin and chromosome culture. Fortunately the mothers had second thoughts, and after reinvestigation at the Children's Hospital they were reassigned female at the ages of 14 and 11 months respectively.

All 6 children in this category are being reared as girls.

Hermaphrodites

There were 19 patients for whom the choice of sex of rearing had to be made. In these cases, it is mainly on the genital morphology that this all-important decision rests.

Quite independent of the size of the phallus, where there is an open vestibule with separate urethra and vagina (Fig. 4), the female sex is chosen. This was the case in 5 of the 9 hermaphrodites we assigned female, and corresponded to the original parental choice, so that no reassignment was

TABLE I. FEMALE PSEUDOHERMAPHRODITISM

Case	Race	Clitoris	Vestibule	Aetiology
1	C	Large	Single opening leading to persistent urogenital sinus into which urethra and vagina open higher up	Congenital adrenal hyperplasia
2	B	Moderate		
3	C	Moderate		
4	C	Moderate		
5	B	Moderate		
6	W	Moderate		Maternal progestin therapy
7	C	Moderate	Separate urethra and vagina	Idiopathic
8	B	Large		

Note: cases 2 and 5 are siblings. C = Coloured; B = Black; W = White.

TABLE II. TESTICULAR FEMINISING (ANDROGEN INSENSITIVITY) SYNDROME

Case	Race	Clitoris	Vagina	Reason for investigation
9	C	Slightly enlarged	Absent	Enlarged clitoris
10	C	Small	Absent	Testis in hernia
11	C	Small	Absent	Testis in hernia
12	B	Small	Absent	Testis in hernia
13	W	Slightly enlarged	Absent	Enlarged clitoris
14	W	Slightly enlarged	Absent	Enlarged clitoris

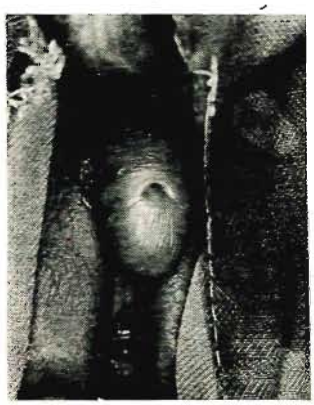

Fig. 4. Case 18. Open vestibule with separate urethra and vagina. In spite of the size of the phallus, the female sex should be chosen here.

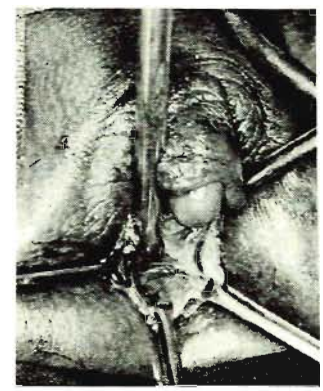

Fig. 5. Case 20. The copious vagina illustrated in Fig. 3 being exposed surgically. U = urethra; V = vagina.

required (cases 15 - 18, Table III). The female sex was also chosen where genitography and/or endoscopy revealed a capacious vagina leading off a single opening representing a persistent urogenital sinus — this applied in 2 patients (cases 19 and 20, Table III). The former had been reared by its parents as a girl, the latter as a boy.

Patient 20 had only a moderate-sized phallus and genitography revealed the capacious vagina illustrated in Fig. 3. This is also shown being exposed surgically in Fig. 5. This baby was reassigned female and Fig. 6 shows the external genital appearance after clitoridectomy.

Table III also illustrates that in these 7 true hermaphrodites for whom the female sex was chosen, exploration and biopsy of the gonads confirmed a preponderance of ovarian over testicular tissue (5 ovaries, 8 ovotestes and 1 testis). This is what one has come to expect in true hermaphrodites where there is a vagina, and would possibly explain why these patients are known to be likely to feminise at puberty in respect of breast development, etc. This is reassuring in that it vindicates one's decision to make such patients girls, the more so since the testes or ovotestes are removed, leaving only the ovaries.

Only when the vagina is absent or rudimentary, and if the phallus is sufficiently large, is the male sex chosen.

Figs 7 and 8 illustrate the external genitalia of 2 such children, each of whom had an adequate phallus and single perineal hypospadic opening which proved to lead to the urethra only. Each had a testis on one side and ovotestes on the other (cases 25 and 26, Table IV). This is typical of the type we made male, and again in only 1 had we to change the original parental choice — from female to male (case 33) (Figs 9 and 10).

TABLE III. HERMAPHRODITES ASSIGNED FEMALE

Case	Race	Phallus	Vagina	Parental choice	Internal morphology	Gonads		Final diagnosis
						Left	Right	
15	B	Large	Separate	Female	Uterus and tubes	O	OT 1 : 1	True hermaphrodite
16	B	Large	Separate	Female	Left unicornuate uterus and tube	O	T	True hermaphrodite
17	C	Large	Separate	Female	Uterus and tubes	OT 3 : 1	O	True hermaphrodite
18	B	Large	Separate	Female	Left unicornuate uterus, bilateral tubes	O	OT 1 : 2	True hermaphrodite
19	B	Large	Off urogenital sinus	Female	Left unicornuate uterus, rudimentary right tube	O	OT 1 : 1	True hermaphrodite
20	B	Moderate	Large, off urogenital sinus	Male	No uterus, rudimentary left tube	OT 1 : 3	OT 1 : 4	True hermaphrodite
21	W	Small	Off urogenital sinus	Deferred	No uterus, bilateral inguinal gonads, epididymis and vasa	OT 1 : 10	OT 1 : 10	True hermaphrodite
22	C	Small	Absent	Male	Right unicornuate uterus and tube	T	A	Mixed gonadal dysgenesis
23	B	Small	Off urogenital sinus	Female	No uterus, bilateral labial testes, epididymis and vasa	T	T	Male pseudohermaphrodite

O = ovary; T = testis; OT 1:1 = ovotestis with proportion ovarian to testicular tissue; A = aplasia.

Fig. 6. Case 20. Appearance 2 weeks after correction by clitoridectomy.

Fig. 7. Case 25. Adequate phallus and a single perineal hypospadic opening leading to the urethra only.

Fig. 8. Case 26. Adequate phallus and a single perineal hypospadic opening leading to the urethra only.

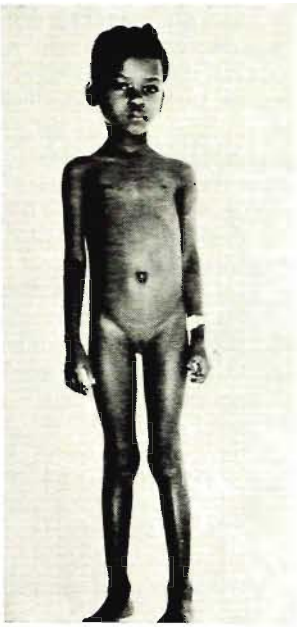

Fig. 9. Case 33. Male pseudohermaphrodite. Parental and hospital assessment was female.

Of the 6 true hermaphrodites reared as male, 1 (case 29) should have been made female. He was originally designated on the strength of biopsy of his right gonad which at the time showed only testicular tissue, and the vagina, uterus and left ovotestis were removed. Numerous operations since have failed to give him an adequate phallus or penile urethra (Fig. 11), and subsequent repeat exploration and biopsy of his right scrotal gonad has revealed this also to be an ovotestis. He is now 14 years old, rather feminine in appearance and build, and psychological assessment with a view to sex reassignment might have to be contemplated.

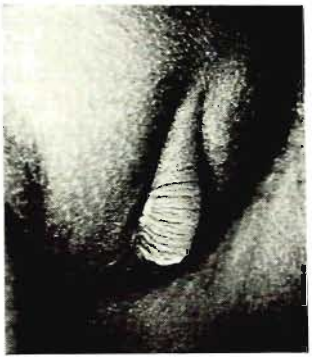

Fig. 10. Case 33. Male pseudohermaphrodite. Internal morphology showed no Müllerian development. Both gonads testes.

Fig. 11. Case 29. True hermaphrodite changed to male. Incorrect decision based on gonadal biopsy. Note the inadequate phallus.

TABLE IV. HERMAPHRODITES ASSIGNED MALE

Case	Parental choice	Race	Internal morphology	Gonads		Final diagnosis
				Left	Right	
24	Male	B	Left unicornuate uterus and tube	O	T	True hermaphrodite
25	Male	B	Left unicornuate uterus and tube	OT 1 : 1	T	True hermaphrodite
26	Male	B	Left unicornuate uterus and tube	OT 1 : 1	T	True hermaphrodite
27	Male	C	Left unicornuate uterus and tube	OT 1 : 1	T	True hermaphrodite
28	Male	B	Left unicornuate uterus and tube	O	T	True hermaphrodite
29	Male	B	Uterus and tubes, vagina	OT 1 : 1	OT 1 : 1	True hermaphrodite (should have been made female)
30	Male	W	Left unicornuate uterus and tube	A	T	Mixed gonadal dysgenesis
31	Male	W	Left unicornuate uterus and tube, vagina	A	T	Mixed gonadal dysgenesis
32	Male	C	No Müllerian elements	T	T	Male pseudohermaphrodite
33	Female	C	No Müllerian elements	T	T	Male pseudohermaphrodite

O = ovary; T = testis; OT 1:1 = ovotestis with proportion ovarian to testicular tissue; A = aplasia.

The other 5 true hermaphrodites, correctly assigned male (cases 24 - 28, Table IV), revealed a preponderance of testicular over ovarian tissue when it came to gonadal biopsy (5 testes, 3 ovotestes and 2 ovaries). The ovaries and ovotestes have been removed. The external genital morphology (adequate phallus and single perineal opening proved on endoscopy and genitography to be urethra only) was essentially the same in these 5 true hermaphrodites, as in the 2 cases of mixed gonadal dysgenesis (cases 30 and 31) and the 2 cases of male pseudohermaphroditism (cases 32 and 33). In the latter 4 cases, no ovarian tissue was found.

From the above it follows that if there is an adequate phallus and no vagina it is realistic, justifiable and probably safe to assign the male sex in hermaphrodites, irrespective of whether they are cases of true hermaphroditism, mixed gonadal dysgenesis, or male pseudohermaphroditism, but if there is an adequate vagina, assignment of the male sex is hazardous and unjustifiable. It is also unrealistic in respect of the extent of surgery required to make the external genitalia conform to the sex assigned and the age by which this can be achieved. It is much easier in this respect to make a female, and this can be done at the age of a few months.

In the absence of either vagina or adequate phallus, the female sex should also be assigned, since it is much easier in adulthood to make an adequate vagina than a penis, and certainly very much easier in infancy to correct the external genitalia to female morphology and so ensure acceptance of the chosen gender by parents and child.

Case 22 (Table III) was the only one in our series falling into this category and who required reassignment from the male sex originally chosen by the parents. As can be seen, she proved to be a case of mixed gonadal dysgenesis and was the only one where chromosome culture revealed a mosaic sex chromosome pattern (XY/YO). Buccal smears were male.

It is unforgivable to condemn such persons to live as males with inadequate masculine equipment, solely on the basis of male genetic or gonadal sex. Extensive studies, notably by Money and his associates,[2] have proved that the gender in which a child is reared is the predominant factor in determining future psychosexual orientation — regardless of chromosomal, hormonal or gonadal identity. Haircut, clothing, name and gender of personal pronouns, toys and type of play, in addition to the anatomy of the external genitalia, are all-important influences in establishing, in early life, the child's conviction as to whether it is a boy or a girl — provided there is no confusion or uncertainty on the part of parents or medical attendants.

SURGICAL PROCEDURES

The surgical procedures aim at abdominal exploration, gonadal biopsy and removal of contradictory internal structures, and corrective surgery to external genitalia.

Some of our patients come from far afield and in these we usually carry out these procedures at the first admission, after conclusion of full investigations. This is current practice at Johns Hopkins Hospital as well, and since the intra-abdominal surgery is of a minor nature in the majority of cases, there is a good reason for doing this and completing the correction of the external genitalia in those made girls, at this time. The handling of the parents is of utmost importance, and since we usually accommodate the mothers (who are invariably still suckling these babies) at the Red Cross Hospital as well, counselling and reassuring them is facilitated.

It is obvious that if correction of the external genitalia can be done before the child and its mother return to their families (which should also not be unduly postponed), their peace of mind about the correctness of what has been done will be best assured. Postponement of these surgical procedures to facilitate easier operating on a bigger child —at the expense of the parents' continued uncertainty and anxiety while living with the still ambiguous-appearing child in a homeland, for example, to await a further long journey and operation at a later date — is unwarranted. This has, however, to be qualified — in the children one decides to rear as boys, it is inadvisable to correct the hypospadias too soon. We have obtained the best results when we have waited until they have reached the age of 3 years, when we correct the chordee, followed by urethroplasty 6 months later.

Abdominal exploration is not required in cases of female pseudohermaphroditism with proven congenital adrenal hyperplasia or a clear-cut history of maternal progestin therapy in pregnancy, but is essential (as in cases 7 and 8, Table I) in the idiopathic variety, to exclude true hermaphroditism. Laparotomy is also not required in cases of the androgen-insensitivity (testicular feminisation) syndrome.

The internal findings in cases of true hermaphroditism are of absorbing interest and infinite variety. They are tabled in Tables III and IV. At one stage of our experience we thought we could predict these with reasonable accuracy, but we have learnt better. It is advisable to have facilities for frozen section available for the cases where there might be doubt as to gonadal identity. However, with experience one can learn macroscopically to distinguish ovarian from testicular tissue with accuracy.

A very valuable guide given to one of us (J.P.R.) by Professor Van Niekerk of Stellenbosch University is that testicular tissue is recognised better by its consistency to touch than by its colour — it is soft and bulges from the edge of its capsule when cut, whereas ovarian tissue is firm and does not bulge. Testicular tissue is usually light brown in colour, whereas ovarian tissue is paler than this if solid, and darker if (as is often the case) it contains small follicular cysts. The line of demarcation in an ovotestis is usually quite well-marked.

From our findings (Tables III and IV) it would appear that the conclusions of other workers have been confirmed:

1. In the presence of a unilateral testis, Müllerian development will not take place on that side (cases 16, 22, 24, 25 - 28, 30 and 31).

2. An ovary is not essential for Müllerian development — in each of the cases of mixed gonadal dysgenesis exhibiting a unilateral testis and contralateral aplastic gonad, a unicornuate uterus was present on the side of the latter (cases 22, 30 and 31).

From our findings of the presence or absence of Müllerian elements in association with ovotestes, we present a third postulate:

3. If more than half an ovotestis is testicular, Müllerian elements will be suppressed on the same side. If any Müllerian development is evident, this will be tubal only. This is suggested by the findings in cases 18 - 21.

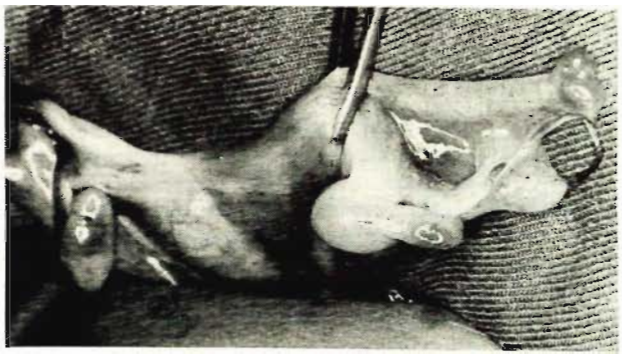

Fig. 12. Case 18. Two-thirds of the right ovotestis was testicular. Fallopian tube only on this side. Left side shows a well-developed unicornuate uterus, tube and ovarian ligament. The gonad here was an ovary.

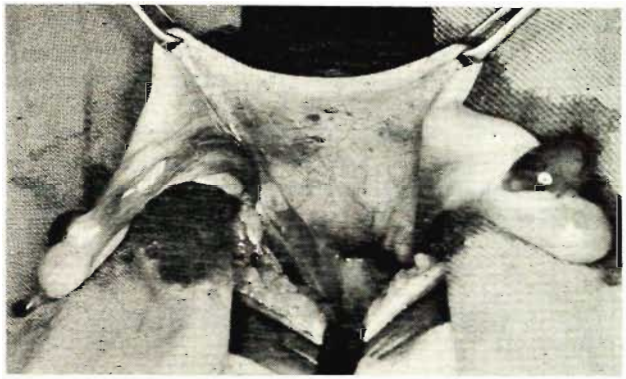

Fig. 13. Case 20. Both ovaries were at least two-thirds testicular. No uterus present.

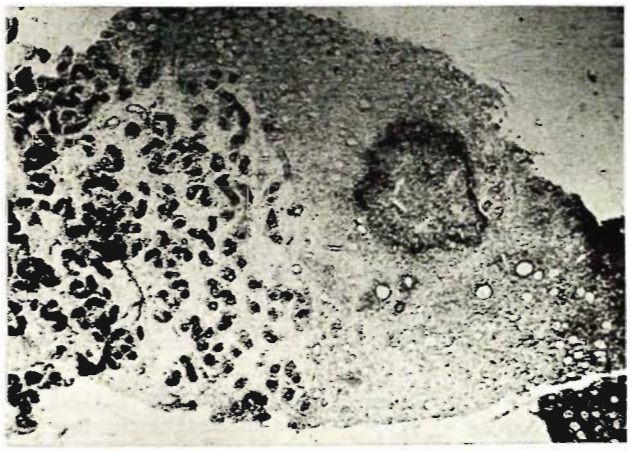

Fig. 14. Case 15. Half or less of the ovotestis composed of testicular tissue.

In case 18 (Fig. 12) two-thirds of the right ovotestis was testicular, and on this side there was a Fallopian tube of which only the proximal (lateral) part was well developed. There was no uterine development on the right, but as can be seen from Fig. 12, there was a well-developed unicornuate uterus, tube and ovarian ligament on the left side where the gonad was an ovary. Case 18 (Fig. 4) again reveals a unicornuate uterus on the side of the left ovary, but no uterus on the side of the right ovotestis, which again was two-thirds testis. Case 20 (Fig. 13) is even more interesting. Both ovaries were at least two-thirds testicular and here no uterus developed, only the large blind vagina (Figs 3 and 5) and a vestigial tube on the one side. On the other hand, where only half or less of the ovotestes have been composed of testicular tissue (case 15, Fig. 14). Müllerian elements have fully developed on the same side (cases 15, 17, 25 - 27 and 29).

Correction of the External Genitalia

Correction to female was required in all the female pseudohermaphrodites. Cases 1 to 7 required reduction of the clitoris as well as incision of the posterior wall of the urogenital sinus to expose the urethral and vaginal openings. Case 8 required only clitoridectomy.

Of the hermaphrodites, cases 15 - 18 and 22 required only reduction of the clitoris, but case 22 will require the construction of a vagina when adult. Cases 19 and 20 required clitoridectomy as well as exteriorising of the vagina from a common urogenital sinus.

Patients operated upon earlier in the series have had a variety of forms of reduction of the clitoris, such as filetting of the corpora with preservation of the glans, recessing of the entire clitoris, etc. but the cosmetic results in these cases have not been entirely satisfactory. Since his return from Johns Hopkins Hospital, one of us (J.P.R.) at first favoured complete clitoridectomy, as is done there, with

Fig. 15. Case 7. The skin on the underside of the clitoris left *in situ*.

results such as shown in Fig. 6 (case 20). Lately, however, he modified this by leaving the skin of the underside of the clitoris and glans and resuturing this in position, with results such as shown in Fig. 15 (case 7).

These operations were originally done some months after the exploratory laparotomy and gonadal biopsy, and the aim was to complete surgery before the age of 18 months. Now both the abdominal and vulval operations are done under the same anaesthetic as soon as full investigation has been completed, with the exception that in the case of patients living in or near Cape Town, the operation is postponed until the age of 6 months.

When a correction to male is made, the hypospadias is corrected in two stages — the first stage (division of chordee) at 3 years of age and the second stage (a modified Denis Browne operation to make a urethra and enable the patient to void through the tip of the penis) 6 months later.

CHROMOSOME STUDIES

Leucocyte Culture

Leucocyte cultures from venous blood were done on all our patients. The results confirmed the findings of other workers. All 8 of the female pseudohermaphrodites had, as expected, a 46,XX karyotype, while all 6 patients with the testicular feminising syndrome were 46,XY — and these investigations were most helpful in finalising diagnosis in both these conditions. The 3 male pseudohermaphrodites were 46,XY and confirmed therefore the histological diagnosis of pure testicular gonads.

Of the 3 patients with mixed gonadal dysgenesis, 2 were unfortunately managed very early in the series and one of them had left Cape Town by the time we wished to study his chromosomes, while the other patient refused the investigation. The third one, the one we reared as female, had the only mosaic karyotype in our series, namely 46,XY/45,XO. (She had a left-sided testis and a right-sided aplastic gonad.)

Our 13 true hermaphrodites all were 46,XX on leucocyte culture — again confirming the findings of other workers.

Tissue Culture

We were able to perform successful tissue culture for chromosomes on 5 of the previous 7 true hermaphrodites with whom we had dealt. The other two failed, but were not done by the same technician. Successful cultures on the testes of 2 of our 3 male pseudohermaphrodites were also obtained and revealed 46,XY chromosomes in each case.

The successful cultures on the 4 true hermaphrodites were all 46,XX, and were obtained as follows: leucocyte cultures were done in all cases, and in case 18 tissue cultures of the ovarian part of the right ovotestis (OT 1 : 2); the testicular part of the right ovotestis (OT 1 : 2), and the left ovary, were also done.

In case 20, tissue cultures of the right gonad (OT 1 : 4) and left gonad (OT 1 : 4) were taken, and in case 27 a tissue culture of the testis was done (the ovotestis had been removed previously).

In case 29, tissue cultures were taken of the testicular part of the right ovotestis, and the ovarian part of the right ovotestis (the left ovotestis had been removed some years earlier before tissue culture had been available).

All these tissues, as mentioned, were cultured successfully and yielded 46,XX chromosomes when harvested. For future cases we will again have full tissue culture facilities available.

REFERENCES

1. Cremin, B. J. (1973): Clin. Radiol. (in press).
2. Money, J., Hampson, J. G. and Hampson, J. L. (1957): Arch. Neurol. Psychiat. (Chic.), 77, 333.