lesser 17-ketosteroid depression or a shorter time of treatment, together with a smaller number of patients.

The fact that some response was obtained, presumably by suppression of adrenal androgen production, supports the view that there is some abnormality in adrenal secretion in these patients (Brooks and Prunty, 1960). The 17-ketosteroids were well suppressed in nearly all patients, but even in spite of this many showed little or no improvement. There is a hint from the results that the response was best in those patients who responded abnormally to corticotrophin.

The effect of added oestrogen in the hirsutism could not be determined and we do not have the impression that under our conditions it was important. Nevertheless it is of theoretical interest that we have observed some synergism with prednisone on 17-ketosteroid depression, though this was relatively small. This effect has also been observed by Armstrong (1955) on combining stilboestrol and cortisone and by ourselves in the congenital type of adrenal hyperplasia (Brooks *et al.*, 1960).

The unfavourable results of ovarian wedge resection in the Stein-Leventhal syndrome on the accompanying hirsutism seems to be a frequent experience (Perloff *et al.*, 1958) though some observers have claimed to find favourable changes (Leventhal and Cohen, 1951). The fact that four out of six patients who were trying to become pregnant after wedge resection did so is in keeping with the 60% occurrence of this result observed by others (see Bailey, 1959).

Summary and Conclusion

The effects of prednisone therapy, usually 10 mg./day and usually combined with ethinyl oestradiol treatment, have been observed in 21 patients with simple hirsutism and three with the hirsute type of Stein-Leventhal syndrome. In six there appeared to be significant improvement, which was much more doubtful in a further nine.

In 10 Stein-Leventhal patients ovarian wedge resection was carried out by our colleagues. The results are discussed. Four out of six patients attempting to become pregnant did so within six months of operation.

In conclusion, while steroid therapy may benefit the occasional patient to a noticeable degree when a reasonably low dosage level is used, we do not feel that it is sufficiently beneficial to justify its use routinely. It is not yet possible to predict whether any particular individual will respond, and the problem of relapse on cessation of treatment also arises.

We are indebted to our several colleagues in the department of obstetrics and gynaecology who kindly performed the ovarian wedge resections.

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SOME EXPERIENCES WITH A NEW ANABOLIC STEROID (METHANDROSTENOLONE)

BY

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Considerable advances have been made in separating the androgenic from the anabolic effects of substances related to testosterone in recent years. Whereas in men there is no real advantage in having an anabolic hormone which is relatively non-virilizing, this is of great practical importance in therapy for women and for children of both sexes.

The development of these new steroids and their applications has been reviewed (Foss, 1959a, 1959b) with preliminary mention of 1-dehydro-17 α -methyl-testosterone.

Chemical Composition

Methandrostenolone (1-dehydro-17 α -methyltestosterone; "dianabol") has the following structural formula, which is compared with that of methyltestosterone. Unlike methyltestosterone, there is double-bonding in the first benzene ring with loss of two atoms of hydrogen from carbons 1 and 2.

In rats its anabolic effect is as great as that of testosterone propionate or norethandrolone, but when tested for its androgenic effect it was approximately 100 times less active than testosterone propionate, and 17 times less active than norethandrolone in castrated rats. In the capon comb test it was 130–170 times less effective than testosterone propionate and 70–90 times less than norethandrolone.

Though these animal experiments with methandrostenolone have suggested that there is a considerable degree of dissociation of anabolic from androgenic effects, the potential hazard still exists in human subjects. In some of the clinical reports of early trials, in which rather large doses were used, mention is made of some virilization, particularly in children.

During the last year an attempt has been made to assess the magnitude of this effect in women, and in children when it was used for the stimulation of growth.

Material and Method

The subjects in this trial consisted of nine children or adolescent patients before growth had ceased (four females and five males) and four adult females. These were selected from hospital out-patients and private patients.

Careful records were made of changes in weight, height, and span; all measurements in each individual patient were carried out on the same instrument, and weights were recorded at the same time of day on the same machine. In some cases serial clinical photographs and skiagrams of epiphyses were taken before and during the course of treatment, and subjects were examined frequently.

At first only scored tablets of 25 mg. were available, but later tablets of 10 mg. were employed. The dose in mg./kg. was at first based on published reports of other anabolic steroids, and one's own experience with these or with methyltestosterone. As the trial proceeded some modification of this schedule was necessary.

Signs of androgenic effect were early lengthening and development of the penis and scrotum in prepuberal cases, early growth of fine hair around the base of the penis or on the pubes; deepening of the voice in adolescent males or in females; and any growth of fine hair on the upper lip or face.

In addition behavioural changes were noted in prepuberal males, such as embarrassment or shyness on being examined or a tendency to erection.

In women with regular menstruation a change in the cycle or delay or suppression of the menses was regarded as an androgenic effect.

Case 1

A female infant aged 1½ years, the youngest child treated, birth weight 7 lb. 8 oz. (3.4 kg.), had always had a small appetite and was of flabby atonic build; weight 21 lb. (9.5 kg.), height 31½ in. (80 cm.). She was given methandrostenolone 25 mg. daily (2.5 mg./kg.). It was very soon apparent that this dose was excessive, as after 14 days she developed reddening, swelling, and discharge of mucus from the vulva. The dose was reduced to 12.5 mg. daily, with resolution of these effects. There was a remarkable change in her appetite. In six weeks of treatment she increased 2½ lb. (1.1 kg.) in weight and 1½ in. (3.8 cm.) in height.

Her progress has been followed for 43 weeks without further therapy, during which time she has had a net gain in weight of 5½ lb. (2.5 kg.) and an increase in height of 4½ in. (11.4 cm.) (Fig. 1). With this brief course of therapy there has been no further sign of precocity or virilization.

Case 2

A boy aged 4 years suffered from frequent attacks of bronchospasm, had a poor appetite, and was generally atonic. He was of normal proportions; weight 36 lb. (16.3 kg.), height 42½ in. (107 cm.). Methandrostenolone 12.5 mg. daily (0.73 mg./kg.) was given for 14 days; the dose was then reduced to 12.5 mg. on alternate days for nine weeks. During this period of 11 weeks he showed a net gain of 4 lb. (1.8 kg.) and his height increased by 1½ in. (3.8 cm.). His appetite was greatly increased and he was always hungry. After this treatment there was minimal lengthening of his penis.

After 40 weeks, however, his genital development was no different from that of any other child of his age, and during this time he had shown a net gain of 7 lb. (3.17 kg.) in weight and had grown 3½ in. (8.9 cm.) (Fig. 2).

Case 3

A boy aged 11 years had suffered with recurrent bronchitis. He had a poorly shaped chest with a marked Harrison sulcus, and his musculature was flabby. His appetite was poor. Weight 67 lb. (30.4 kg.), height 54 in. (137 cm.). He

FIG. 1.—Case 1.

FIG. 2.—Case 2.

FIG. 3.—Case 3.

was given methandrostenolone 50 mg. daily (1.65 mg./kg.) for five weeks only. At the end of this period he was more robust and was always hungry. During this time he had gained 9 lb. (4.1 kg.) in weight and grown $\frac{1}{2}$ in. (1.27 cm.).

There was minimal penile lengthening with fine hair around the base of the penis. Since withdrawing treatment there has been no further genital change or growth of pubic hair. Subsequent growth has been excellent, and in 46 weeks from starting therapy there was a net gain of 10 lb. (4.5 kg.) in weight and he had increased by $2\frac{1}{2}$ in. (6.7 cm.) in height (Fig. 3).

Case 4

This child's growth and development had been followed since February, 1956, when at the age of 8 years 10 months he weighed 44 $\frac{1}{2}$ lb. (20.2 kg.) and measured 44 $\frac{1}{2}$ in. (113 cm.) in height—normal 58 lb. (26.3 kg.) and 51 in. (130 cm.). He was a healthy active child of rather short parents, and no organic cause was found to account for his small stature. After two years he was so concerned about his small size that it was decided to stimulate his growth with norethandrolone. A 10-weeks course of 10 mg. daily (0.45 mg./kg.) produced an acceleration of growth with a weight gain of 7 lb. (3.2 kg.) and an increase in height of 1 in. (2.54 cm.).

A second course of norethandrolone, increased after one month to 0.74 mg./kg. and maintained for nine weeks,

FIG. 4.—Case 4.

produced a much smaller response and he grew less than $\frac{1}{2}$ in. (1.27 cm.) in three months.

At age 11 $\frac{1}{2}$ years he was given methandrostenolone 25 mg. daily (0.95 mg./kg.) for a month and 12.5 mg. daily (0.43 mg./kg.) for a second month, during which time there was a gain of 7 $\frac{1}{2}$ lb. (3.4 kg.) in weight and his height increased by 1 $\frac{1}{2}$ in. (3.8 cm.) (Fig. 4).

At the end of the treatment with methandrostenolone, when he was 11 years 8 months, there was minimal lengthening of the penis with fine short basal peripenile down. He was also becoming self-conscious when weighed and measured, and attempted to cover his genitalia with his hands. After this the growth rate diminished, but, nevertheless, during the norethandrolone period he grew 2 in. (5.1 cm.) in 10 $\frac{1}{2}$ months, and from the onset of methandrostenolone therapy he grew 2 $\frac{3}{8}$ in. (7.3 cm.) in 11 $\frac{1}{2}$ months.

Case 5

A foster child aged 11 $\frac{1}{2}$ years, whose growth had been followed since he was 5 $\frac{1}{2}$ years, was about 4 $\frac{1}{2}$ in. (11.5 cm.)

below the normal average height, but the rate of growth was natural. He was active, fit, and healthy, but was inclined to be a problem child and was now very conscious of his small size in relation to boys in his class. He weighed 57 lb. (25.8 kg.), height 51 $\frac{1}{2}$ in. (131 cm.), span 50 in. (127 cm.)—normal: weight 74 $\frac{1}{2}$ lb. (33.8 kg.), height 56 in. (142

FIG. 5.—Case 5. Before (left) and after (right) 11 weeks' treatment with methandrostenolone 0.48 mg./kg.

cm.), span 56 $\frac{1}{2}$ in. (144 cm.). His proportions and genital development were normal for those of a boy of about 9 $\frac{1}{2}$ years. X-ray examination of his epiphyses showed retardation equivalent to that of a boy of 9–10 years.

Treatment with methandrostenolone 12.5 mg. daily (0.48 mg./kg.) was started, and after 11 weeks there was very minimal lengthening of the penis (Fig. 5) and he had gained 4 lb. (1.8 kg.) in weight and increased in height and span by $\frac{3}{8}$ in. (1.9 cm.). Treatment was stopped after 16 weeks. Penile lengthening was now definite, there was fine downy hair

FIG. 6.—Case 5

FIG. 7.—Case 5. Showing epiphysial development after six months' treatment with methandrostenolone.

over the pubes around the base of the penis, and early voice-change was apparent.

A second course was started, 10 mg. daily for one month (0.3 mg./kg.). His subsequent growth is shown in Fig. 6. Serial radiography showed quite an appreciable advance in maturation of the epiphyses and corresponded to those of a boy of 11 years (Fig. 7). The net gain in weight was 11½ lb. (5.2 kg.) and growth 2½ in. (7 cm.) during six months' treatment.

Case 6

This girl's birthweight was 4 lb. 2 oz. (1.9 kg.), and owing to her diminutive stature and rather difficult childhood she had been under observation since birth. At the age of 9 years she had the appearance of progeria, but investigation showed no abnormalities; weight 37 lb. (16.8 kg.), height 45½ in. (116 cm.).

On June 4, 1957, it was decided to stimulate growth with thyroxine and methandrostenolone. There was a satisfactory response, and in the next 17 months she grew 6 in. (15.2 cm.). Therapy was changed to norethandrolone 10 mg. daily (0.45 mg./kg.) and continued intermittently for six months, during which time she had grown another 1½ in. (3.2 cm.).

When she was 11½ years methandrostenolone 10 mg. daily (0.37 mg./kg.) was substituted; weight 60 lb. (27.2 kg.), height 54½ in. (138 cm.). After 13 weeks she had increased by 1½ in. (3.2 cm.) in height, and treatment was stopped. There was no facial hair; she had a normal voice, quite thick pubic hair, a trace of axillary hair, and there had been no change in epiphysal maturation in three months (Fig. 8).

FIG. 8.—Case 6.

Case 7

This was a remarkable child with a rare type of dwarfism. 5 lb. (2.27 kg.) at birth, she had a history of recurrent chest infection since the age of 1 year. She was shown to have a ventricular septal defect with mild pulmonary hypertension, dwarfism, osteoporosis, and latent renal failure. Puberty occurred normally, and the menarche was at 12½ years. X-ray examination of the skull showed calcification of her basal ganglia. Her case has already been published (Benson, 1959).

At 14 years she was a diminutive girl with small breasts and well-developed pubic and axillary hair and proportionate dwarfism: weight 50½ lb. (23 kg.), height 46½ in. (118 cm.), span 51½ in. (130 cm.)—normal: weight 101 lb. (45.8 kg.), height 61 in. (155 cm.). Menses were regular. X-ray pictures showed that epiphyses of the metacarpals and phalanges were beginning to unite, but the iliac-crest ossification was not present. All the bones were very small for her age.

An attempt was therefore made to stimulate growth, though she had been

treated previously with methyltestosterone and had grown only ½ in. (1.27 cm.) in the preceding two years.

Methandrostenolone was started on July 7, 1959, 10 mg. daily (0.43 mg./kg.) intermittently. After six weeks she had grown ½ in. (1.6 cm.). Her menses in July and August were suppressed during treatment, but started again on September 19, when treatment was withheld.

Case 8

At the age of 17½ this girl weighed 82 lb. (37.2 kg.), height 53 in. (135 cm.), span 54½ in. (138 cm.) and looked about 12–14 years, with no breast development and early labial hair. She was believed to be a case of ovarian dysgenesis with a high level of F.S.H., but both buccal cells and polymorphs were of the normal female type.

X-ray pictures of the epiphyses showed retarded development, with a bone age equivalent to that of a girl of 14. It was decided to try to stimulate growth for as long as possible with methandrostenolone and when the epiphyses had closed she would be treated with oestrogens and progesterone.

FIG. 9.—Case 8.

Methandrostenolone was started on April 7, 1959, 12.5 mg. daily (0.34 mg./kg.). After seven weeks she had gained 10 lb. (4.54 kg.) but grown only ½ in. (0.64 cm.). The dose was increased to 0.5 mg./kg. for a month and continued intermittently with varying doses. 34 weeks after starting treatment she had gained 22 lb. (10 kg.) in weight and had grown 1½ in. (4.45 cm.) (Fig. 9). There was minimal breast-budding, with a trace of hair at the corners of her upper lip. Pubic hair had increased and her voice was very slightly husky. Epiphysal development had scarcely altered in this time.

Case 9

An intelligent articulated accountant was first seen at the age of 21½ years. He weighed only 105 lb. (47.6 kg.), but was of average height 66½ in. (170 cm.), span 66½ in. (169 cm.). His face and body were completely hairless and his

FIG. 10.—Case 9. Before (left) and after (right) 14 weeks' treatment with methandrostenolone 1 mg./kg.

skin was pale, smooth, and soft. He looked like a tall boy of about 12 years with no sign of genital development and with two infantile testes in the scrotum.

He had bilateral optic atrophy and bitemporal hemianopia, and an x-ray examination showed a large sella without erosion of the clinoids and no evidence of calcification in the pituitary region. Bone age corresponded to that of a boy of 12 years. 17-Ketosteroids were 2.9 mg./g. creatinine. Though there was slight evidence of impairment of thyrotrophic and corticotrophic factors the major feature was gonadotrophic deficiency, and while awaiting surgery it was decided to observe the effects of methandrostenolone.

After three weeks of 25 mg. twice daily (1 mg./kg.) erection occurred five or six times daily and minimal penile lengthening was noted. After a month the nipples were tender and slight subareolar thickening was apparent. After six weeks there was no increase in level of 17-ketosteroids (0.86 mg./g. creatinine). After 14 weeks on this dose he had gained 15 lb. (6.8 kg.) in weight and grown $\frac{1}{2}$ in. (1.9 cm.) in height. The serial photographs show the slight but definite androgenic effects (Fig. 10).

Methandrostenolone was continued throughout the period of operation and convalescence and then methyltestosterone was substituted in the same dosage.

Adult Female Cases

Case 10.—A woman aged 25, height 63 in. (160 cm.), had had both ovaries removed at 12 years for bilateral dysgerminoma and had subsequently developed a normal adult figure with oestrogens and cyclical progestogen therapy, weight 107 lb. (48.5 kg.) and wished to increase her weight. She was given a high-protein diet and methandrostenolone 0.5 mg./kg. for 12 weeks, during which time she gained 8 lb. (3.63 kg.). Her menses remained regular during this period, but she developed a greasy skin and several acne spots on her back. There was no hirsuties or change in her voice.

Case 11.—A woman aged 60 with osteoporosis of the spine, weighing 104 lb. (47.2 kg.), was given methandrostenolone 1.6 mg./kg. for 35 weeks except for an interval of six weeks. During this time there was only a net gain of 5 lb. (2.26 kg.). She has had no hirsuties or voice change at all up to the time of writing.

Case 12.—A woman aged 36 with regular menstruation was given methandrostenolone 25 mg. daily (0.5 mg./kg.) for 30 days. There was no suppression of menses and no sign of hirsuties or voice change.

Case 13.—A woman aged 43 who had had a radical mastectomy for breast carcinoma followed by deep x-ray therapy was given methandrostenolone 25 mg. twice daily (1 mg./kg.) for six weeks during which time she gained 4 lb. (1.8 kg.) in weight, but there has been no voice change or hirsuties, and her menses have continued without any alteration in the cycle or amount of loss.

Discussion

The effects of this anabolic steroid on the stimulation of growth are impressive; its action in this respect is extremely rapid and continuous during the short periods of therapy and seems to accelerate the general trend

of growth when therapy is withdrawn. One of its main influences is the increase in appetite and a considerable gain in weight.

In the preliminary trials it soon became obvious that dosage was too high, and this was largely due to the fact that only tablets of too large a dose were then available. For children 5-mg. tablets are much more generally useful, as a dose of 0.1–0.3 mg./kg. should be sufficient. Short courses of treatment on these lines, repeated as necessary after an interval, will be satisfactory in most cases. Serial skiagrams are necessary to ensure that the bone age is not advanced by treatment, particularly when available linear growth is limited on first investigation of epiphyseal maturation.

The use of methandrostenolone in premature infants may be of value in promoting protein anabolism at a phase when normally the infant should be growing at a greater rate than at any other time in life.

Metabolic balance studies have shown that methandrostenolone causes nitrogen retention with some retention of sodium and potassium during therapy (V. Wynn, 1958, personal communication).

Burke and Liddle (1960), in short-term metabolic studies in man, have assayed various synthetic analogues of testosterone for nitrogen-retaining activity, and methandrostenolone was shown to be about five times as potent as norethandrolone or methyltestosterone. Its stimulus to growth may be relative to the potency of its anabolic effect, and is similar to that which occurs with methyltestosterone therapeutically or with the normal androgens at puberty. However, largely bereft of its androgenic effect, it is possible that methandrostenolone may not cause premature closure of epiphyses, which is the normal result of puberty. Only long-term studies will show whether intermittent therapy with methandrostenolone in anabolic but relatively non-virilizing doses will produce growth ultimately greater than would be expected. Previously it has always been argued that therapy with methyltestosterone only produced an acceleration of growth similar to the puberty spurt, with an ultimate height the same as that which would have occurred without it, in the course of time.

It is likely that its effect in this respect is dependent on the complementary anabolic actions of thyroid hormone and insulin with adequate diet; but the absence of growth hormone may not matter, as with thyroid and methyltestosterone Hubble (1957) stimulated growth in primary hypopituitary dwarfs.

It is interesting to wonder whether the powerful anabolic stimulus of methandrostenolone would effect ultimate growth in dwarfism associated with mongolism, congenital heart disease, chronic renal disease, and the malabsorption syndrome.

Cases Treated Before Cessation of Growth

Case No.	Age	Sex	Weight		Height		Initial Dose mg./kg.	Growth with Methandrostenolone				Subsequent Growth from Onset		
			lb.	kg.	in.	cm.		Weeks	% Wt.	in.	cm.	Weeks	in.	cm.
1	1½	F	21	9.5	31½	80	2.50 (1.25)	6	12	1½	3.8	43	4½	11.4
2	4	M	36	16.3	42½	107	0.73	11	11	1½	3.8	40	3½	8.9
3	11	M	67	30.4	54	137	1.65	5	13	+	1.27	46	2½	6.7
4	11½	M	58	26.3	48½	123	0.93	8	13	1½	3.8	48	2½	7.3
5	11½	M	57	25.8	51½	131	0.48	26	20	2½	7.0	48	4½	10.8
6	11½	F	60	27.2	54½	138	0.37	13	7.5	1½	3.2			
7	14	F	50½	23.0	46½	118	0.43	6	0	½	1.6			
8	17½	F	82	37.2	53	135	0.34	34	28	1½	4.45			
9	21½	M	105	47.6	66½	170	1.00	14	14	½	1.9			

The accompanying Table shows that the unnecessarily high doses at first used in Cases 1, 2, and 4 produced 1½ in. (3.8 cm.) gain in height in 6, 11, and 8 weeks respectively, together with a percentage gain in weight of 12, 11, and 13. In these three cases and Case 3 there was definite slight androgenic effect during the course of treatment, which, however, did not progress when treatment was withdrawn. Subsequent growth continued at a very much higher rate than in untreated children of the same age.

In Cases 5, 6, and 8, in which doses of 0.34–0.48 mg./kg. were used, there was still a very useful stimulus to growth on longer or intermittent therapy with gains of 2½ in. (7 cm.) in 26 weeks, 1½ in. (3.2 cm.) in 13 weeks, and 1½ in. (4.45 cm.) in 34 weeks, and a corresponding net percentage gain in weight of 20, 7.5, and 27. In Case 7 the growth had been only ½ in. (1.27 cm.) in the preceding two years, and the epiphyses were showing signs of incipient closure, and yet the patient gained ½ in. (1.6 cm.) in six weeks without a net gain in weight.

Evidence of commencing puberty was noted in Case 5, and in Case 7 two periods were suppressed during therapy, but normal rhythm was restored on withdrawal. In Case 8 there was slight increase in pubic hair and some dark fluff at the angles of the mouth with early areolar budding.

In Case 9, a young man of 21½, with the pituitary tumour and secondary hypogonadism, was an excellent test subject for evidence of androgenicity. On a continuous dose of 1 mg./kg. daily, objective signs of secondary sexual development were slight after three months. After a further three months the penis and scrotum were larger and scanty pubic hair was 1 in. (2.54 cm.) long and his voice was beginning to deepen. Treatment was then changed to methyltestosterone, and after seven weeks he experienced his first emission.

In adult females, Case 10 showed no suppression of menstrual rhythm while on her cyclical oestrogens and norethisterone. There was no sign of hirsuties or change of voice during 12 weeks' therapy with 0.5 mg./kg., but she did have some acne on her back.

An older woman, Case 11, was free from voice-change or hirsuties after continuous therapy with 1.6 mg./kg. for 35 weeks. Two other women given short periods of therapy for four to six weeks were not virilized in any way.

It would seem, therefore, that methandrostenolone in doses known to produce a good anabolic effect is almost free from androgenicity in women. On the other hand, there is no doubt that, in children, minimal signs of incipient virilization may be noted if the dose is above 0.5 mg./kg. and maintained for more than short periods. As a stimulus of growth 0.2–0.5 mg./kg. is very satisfactory, and after about one to two months' therapy should preferably be withdrawn for three to four months.

Reports from the Continent (Pittman, 1959) claim that no virilization was seen in women with carcinoma of the breast or cervix treated with 200 mg. of methandrostenolone daily for four weeks. Most investigators used doses much larger than necessary at first, but it was reported that in children there was no significant virilizing action with daily doses of 1–2 mg./kg. (Pittman, 1959). There is little doubt, however, that these doses are much too big and that, if continued, will produce virilization. Though no signs of toxicity were seen even in adults given prolonged therapy, the

possibility of cholestatic jaundice similar to that which sometimes follows treatment with norethandrolone or methyltestosterone (Foss and Simpson, 1959) should be remembered.

Summary

During the past year studies have been made on a group of nine children or hypogonadal patients and four adult females. Methandrostenolone has been shown to have a powerful anabolic effect, stimulating growth with increase in weight and height. There was evidence of continued acceleration of the growth pattern after withdrawal of therapy. For growth stimulation, doses of 0.25–0.5 mg./kg. were effective when given for short periods of four to six weeks; it may then be withdrawn for three to four months before giving a second course of treatment. However, on this regime signs of virilization were minimal, and in view of the results achieved they are of small concern. Smaller doses may well be adequate.

Even when at first unnecessarily large doses were used there were no prolonged androgenic effects.

Adult women showed no virilization with doses up to 1.6 mg./kg., and it is unlikely that higher doses are necessary.

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"One hundred and twenty years ago, in 1839, in a English city, expectation of life was very different from what it is to-day and very different for different classes. A baby born in a labourer's family might expect to live on an average 23.8 years; in the same city in a tradesman's home the baby might expect to live 30.8 years; if born in the home of the privileged gentry, its expectation of life was 48.6 years. By the turn of the century, the average figure for all classes had just passed that for the privileged of sixty years previously and stood at 48.5 for males and 52.4 for females. Judged by the criterion of expectation of life, to-day's most privileged babies are born in Holland, Sweden, and Norway, where the figures stand at 71, 70.5 and 69.3 respectively, closely followed by Australia, Denmark, New Zealand, Switzerland, United Kingdom, and United States of America. The underprivileged are born in India, where expectation of life at birth in 1950 still stood at 32.5 years, and India stands in this respect only at the bottom of a list of countries for which statistics are available. Where there are no statistics, it is likely that conditions are worse; for example, the indigenous population of Northern Rhodesia was estimated to have a crude death rate in 1950 of 32.2. Indonesia at the same time had an estimated rate of 20, and of this latter country it had been stated that an infant child dies every minute and a mother dies in childbirth every quarter of an hour. . . ." (Professor A. D. Munrow, University of Birmingham, at Unesco International Conference on the Contribution of Sports to the Improvement of Professional Abilities and to Cultural Development, Helsinki, August, 1959.)