FURTHER EXPERIENCES WITH ETHINYL OESTRADIOL IN THE SUPPRESSION OF LACTATION

BY

T. N. A. JEFFCOATE, M.D., F.R.C.Sed., F.R.C.O.G.

AND

BETTY HARGREAVES, M.B., Ch.B., M.R.C.O.G.

(From the Department of Obstetrics and Gynaecology, University of Liverpool)

In a previous communication (Jeffcoate *et al.*, 1948) it was mentioned that some writers had suggested that ethinyl oestradiol when administered orally has a more prolonged action than other oestrogens. To test the validity of this suggestion further clinical trials have been carried out, the suppression of lactation again being the test object. The total dose administered was of the same order as in the previous trials, but it was all given in one or two days instead of being spread over seven days. Single doses were impracticable, since it would have meant that a patient took a very large number of 0.05-mg. tablets at one time. In one scheme the total dose was given during one day and usually within twenty-four hours of delivery; in the second the same total dose was given, half during the first day and half during the fourth day of the puerperium. Thirty-seven patients were treated, and the results are classified as excellent, good, fair, or poor, according to the criteria set out previously.

Scheme I

(a) *Technique*.—Eleven tablets (0.55 mg.) during the first day, administered in three doses at four-hourly intervals. *Results*: Six patients were treated, two with excellent results. Two had fullness of the breasts with pain on the fourth and fifth days, one had free secretion of milk on the fourth and fifth days, and a sixth complained of fullness and pain on the sixth day. A supplementary course of treatment with 0.1 mg. of ethinyl oestradiol was necessary in these four cases. (Two excellent, four poor.)

(b) *Technique*.—Fifteen tablets (0.75 mg.) during one day, administered in three doses at four-hourly intervals. *Results*: Seven patients were treated, one with excellent result. Two experienced fullness of the breasts with slight discomfort—on the second day in one case and on the fourth day in the other. In the latter, treatment did not begin until the second day of the puerperium. Four patients showed a poor response. In two of these, symptoms arose on the sixth and seventh days and necessitated further treatment. The two others started treatment on the second day and had pain and fullness on the following day. (One excellent, two fair, four poor.)

(c) *Technique*.—Twenty tablets (1 mg.) during the first day, administered in four doses at four-hourly intervals. *Results*: Four patients were treated, one with excellent result. A second patient had pain and fullness on the fourth day, a third had similar symptoms on the eighth day, whilst a fourth had a free flow of milk from the sixth to twelfth days. (One excellent, three poor.)

Scheme II

(a) *Technique*.—Six tablets (0.3 mg.) first day, five tablets (0.25 mg.) fourth day—total, 11 tablets (0.55 mg.). *Results*: Six patients were treated, three with excellent results and two with good results. Of the latter, one had slight secretion on the fourth and the other on the fifth day. A sixth had minimal discomfort on the second day only. (Three excellent, two good, one fair.)

(b) *Technique*.—Eight tablets (0.4 mg.) first day, seven tablets (0.35 mg.) fourth day—total, 15 tablets (0.75 mg.). *Results*: Seven patients were treated, two with excellent results. Four cases had moderate fullness of the breasts on the fourth day,

relieved by the second dose, whilst the seventh case had fullness and pain on the fourth day. (Two excellent, four fair, one poor.)

(c) *Technique*.—Ten tablets (0.5 mg.) first day, ten tablets (0.5 mg.) fourth day—total, 20 tablets (1 mg.). *Results*: Seven patients were treated, with excellent results in three cases and with a good result in another two. The remaining two cases had pain and fullness of the breasts—one on the fourth and the other on the sixth day. Both required further treatment. (Three excellent, two good, two poor.)

Conclusions

The results of these trials may be summarized by saying that ethinyl oestradiol in relatively large doses given over a short period or at long intervals is unreliable in suppressing lactation, whereas in divided doses spaced over several days it was previously shown to give excellent or good results in a high percentage of cases. With a total dose of 0.55 to 0.75 mg. given during the first seven days of the puerperium an excellent or good response was noted in 24 out of 27 cases in the previous trials. In this series, 0.55 mg. to 1 mg. administered during a period of 12 hours produced only four good or excellent results in 17 cases. When it was divided and given half on the first day and half on the fourth day of the puerperium the effect was satisfactory in 12 out of 20 cases.

The results reported here compare so unfavourably with the earlier ones that it seems permissible to conclude that they offer little evidence to support the idea that ethinyl oestradiol is absorbed or utilized comparatively slowly and that its effect is prolonged. If it has these properties, then they are not so strongly developed as to make the administration of single massive doses, or large doses at infrequent intervals, an efficient method. As in the case of other oestrogens, smaller doses given regularly during several days are the most effective.

REFERENCE

Jeffcoate, T. N. A., Hargreaves, Betty, Lister, Ursula M., and Roberts, H. (1948). *British Medical Journal*, 2, 809.

METATARSUS QUINTUS VALGUS

BY

HORACE DAVIES, Ch.M., M.Ch.Orth., F.R.C.S.

Orthopaedic Surgeon, St. Catherine's Hospital, Birkenhead,
and Whiston Hospital, Lanes

Much individuality appears to exist in the shape of the fifth metatarso-phalangeal junction. Rarely do we see a foot with its outer border prolonged straight forward along the little toe. The head of the metatarsal interrupts this line by protruding outwards, and the axis of the little toe is usually directed inwards. Most feet therefore exhibit a bunionette, or, as it has been called, a tailor's bunion, to a greater or less degree. Rarely, however, does it give rise to symptoms. A bunionette is not uncommonly seen in combination with pes and hallux valgus and general splaying of the forefoot, and is therefore regarded as a secondary deformity in these cases. Chronic irritation due to pressure upon the lateral surface of the foot in the cross-legged or sartorial position is also to be considered as a causative factor, for it was this that gave rise to the name "tailor's bunion." The case of bilateral bunionette described below appeared as a primary and independent deformity, and the suggestion is made that such a condition can occur as a distinct clinical syndrome.

A girl aged 9 came to the clinic complaining of painful swellings at the bases of the little toes. They had been

noticed about two years previously, but had remained symptomless until the last six months. Examination revealed unusually prominent swellings over the fifth metatarsophalangeal joints, with the little toe directed inwards, following the axial deviation of the outer three digits. Radiographs show a varus position of the little toe, adaptive changes in the basal phalangeal and metatarsal epiphyses, and outward splaying of the fifth metatarsal. Clinically and radiologically the condition therefore resembles metatarsus primus varus.

Aetiology

In considering the cause of this condition we must refer to the embryology of the foot. The mesodermal concentrations destined to be the metatarsals are laid down radially, diverging towards the convex border of the limb bud. This fanwise arrangement persists up to about

the 20-mm. stage. At this time we see the differentiation and development of the transverse metatarsal ligament, and this restraining rein thrown across the heads of the developing metatarsals appears to exert a converging influence. Development proceeds with the metatarsals assuming the more parallel positions they occupy in the adult. Imperfect attachment of the transverse metatarsal ligament to the fifth metatarsal could allow primitive divergence to persist, which I would suggest is the primary error in this condition.

In the early stages the developing digits radiate from the convex border of the limb bud, following the lines of the diverging metatarsals, and their realignment to the adult position is difficult to explain. It would appear, however, that two factors are at work: (1) the inherent human pattern responsible for the blue-print of our shape and size, and (2) mechanical forces.

In considering these mechanical forces we see that the changing shape of the developing foot plays an important part. The convex border of the embryonic foot presents at first a large arc of a small circle. As development proceeds this arc expands, gradually transforming itself into a wider arc of a larger circle, with predominant expansion of the pre-axial side. This expansion of the arc brings the radiating toes into more parallel positions. Coinciding with this, the developing intrinsic and extrinsic muscles begin to exert their influence. The flexor longus digitorum, pulling from the inner margin of the foot, has an adducting effect upon the third, fourth, and fifth toes. This pull is

exerted mainly upon the terminal phalanges. The toes are pulled into their parallel positions, but in many individuals this pull continues beyond the normal, and the terminal phalanges are adducted and flexed. The intrinsic muscles, especially the pedal interossei, should prevent this, as one of their little-appreciated functions is to extend the two terminal phalanges. There thus develops a minor tug-of-war between the strong adduction flexing action of the long flexor and the relatively weak degenerating interossei. Now if the primitive divergence of the fifth metatarsal persists the obliquity of the flexor pull is increased and the whole fifth digit becomes adducted.

Treatment.—Rarely do these cases require active treatment other than the provision of well-fitting shoes. Bunionectomy or trimming of the lateral surface of the metatarsal head may be necessary in pronounced cases with clinical symptoms. If the primary factor is the abduction of the metatarsal shaft, osteotomy should theoretically be the treatment of choice, but in practice, as for metatarsus primus varus, this procedure is both unnecessary and often unsatisfactory.

Summary

Unusual prominence at the fifth metatarsophalangeal joint is either a primary or a secondary deformity. If it occurs as an independent condition it constitutes a syndrome, which should be described as metatarsus quintus valgus. The underlying basic congenital error is the persistence of the embryonic splaying of the fifth metatarsal, probably due to incomplete or imperfect development of the transverse metatarsal ligament.

Medical Memoranda

Sprue-like Mouth and Swelling of Lips as a Manifestation of Streptomycin Sensitivity

Many toxic manifestations of streptomycin have been described, but the following experience seems to add one more to the list of "dangers."

CASE HISTORY

A man aged 57, a wine merchant of moderate habits, was recently seen by me for chronic pulmonary tuberculosis. There was infiltration of both lungs, with cavitation on the right, and it appeared from the history and from his subsequent response to conservative treatment that he was going downhill. It was therefore decided to try streptomycin. The streptomycin used was streptomycin calcium chloride complex, and the amount given was 1 g. daily in two doses. One month later the E.S.R. still remained high (95 mm. in one hour), but there was considerable subjective improvement. He, however, complained of some temporary giddiness following injections which did not amount to vertigo.

Five weeks after the beginning of treatment he complained of slight weakness of the legs, particularly noticeable on climbing stairs, and on the same day there was a feeling of numbness of the lips with a slight swelling of the mucous membranes. Within two days the patient complained of a feeling of thickness of the tongue, which subsequently became furred and after a few days ulcerated; at the same time there was some superficial ulceration of the inner aspects of the cheeks, the whole picture resembling severe sprue except that the lips were swollen.

Professor G. Ransome saw him at this stage and suggested that a vitamin-B deficiency factor might be contributory. Sensitivity was suspected in view of the lip-swelling. The streptomycin was stopped and the patient was given daily five 4-ml. injections of "plexan" and an adequate dosage of vitamin-B complex. The condition slowly subsided over a period of three weeks, during which time he experienced considerable pain.

Three weeks after stopping streptomycin it was decided to try a test dose to establish whether or not this was indeed a manifestation of streptomycin sensitivity. Three hours after injection of 0.5 g. the lips and tongue swelled, the pulse rate increased, and the patient felt warm all over and itchy. There was a migraine-like headache. Two mg. of adrenaline in oil was given and 50 mg. "benadryl" thrice daily, this being continued for a few days. The immediate distress was relieved within a few hours, but the swelling of the lips and