Date	Occult Blood Test (Faeces)		Haemoglobin (Blood) Per Cent.
	Guaiaac	Haemato- porphyrin	
September 23—haematemesis			(No iron or trans- fusion given)
October 9	2+	2+	38
" 13	2+	2+	39
" 15	+	+	38
" 16	+	+	36
" 19 magnesium tri- silicate commenced	+	+	38
" 20	—	+	45
" 21	—	—	55
" 24	—	—	56
" 26	—	—	55
" 31	—	—	60
November 5	—	—	70
" 9	—	—	75

CASE III.—*Jejunal Ulcer*

J. B. B., aged 48, had suffered from dyspepsia since 1925. In 1927 appendicectomy was performed. In 1930 an investigation revealed hyperchlorhydria and gastric bleeding. In 1931 he had posterior gastro-jejunostomy for a chronic prepyloric ulcer. In 1933 the ulcer was still active, and a partial gastrectomy was undertaken. In 1934 there were daily bouts of left epigastric pain, not closely related to meals. The patient had severe constipation, general exhaustion, and loss in weight. An x-ray examination showed the deep crater of a jejunal ulcer. There was much occult blood in the faeces.

On the routine treatment previously outlined, and a dose of 5 grains (anhydrous weight) of the trisilicate between every feed, the pain quickly disappeared and the general condition improved. Although the pain had recurred daily for more than six months, he was able to start convalescence with a pain-free abdomen and a radiologically normal jejunum after sixteen days of treatment.

The clinical results were equally satisfactory in the remaining cases, and further detailed descriptions would be wearisome. Synthetic hydrated trisilicate of magnesium quite clearly supplied an effective medicinal control for all. The special features of its employment are: (1) The combination of three therapeutic actions in a single substance—namely, antacid, antipeptic, and antitoxic, each of which fulfils a useful role in the stomach and duodenal bulb. (2) A sustained action whereby hydrochloric acid, destructive ferments, and toxins can be removed continuously for several hours after the administration of a single dose. (3) The possibility of a local therapy at the ulcer base independently of changes occurring in the gastric contents as a whole. (4) Freedom from the risk of inducing toxic alkalosis.

Summary

1. Synthetic hydrated magnesium trisilicate possesses antacid and general adsorbent properties, readily applicable to the treatment of chronic peptic ulceration and hyperchlorhydric dyspepsia (discussed more fully in the two preceding papers).

2. It differs from all other antacids in clinical use in the vigour of its adsorbent action, as measured by the methylene-blue method (Table I).

3. Its neutralizing action continues for several hours even in the presence of an excess of acid, and exerts a sustained control over gastric hyperacidity (test meal analyses, Table II, and curves).

4. This prolonged neutralizing action enables a minimum amount of mineral base to control hyperchlorhydria

continuously. The quantity required is far below that which has been known to produce toxic symptoms of alkalosis. The trisilicate itself is insoluble in water and weak alkalis, so that any unused excess remains unabsorbed.

5. The possible local therapeutic action in the ulcer crater is discussed.

6. A series of successfully treated cases of chronic peptic ulceration is quoted in which the only antacid substance administered was synthetic hydrated trisilicate of magnesium.

OESTROGENIC ACTION OF COMPOUNDS OF THE ANDROSTERONE-TESTOSTERONE SERIES

BY

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It has been known for some years that extracts of testis and male urine may show oestrogenic activity,¹ but this has usually been ascribed to the presence in the extracts of oestrogenic substances, probably of the oestrone group, in addition to male hormone. The fact that large amounts of oestrone can be isolated from stallion urine by mild chemical treatment is, of course, strong evidence in favour of this view,² but a purely oestrogenic substance has never actually been isolated from other male mammals. It is now recognized that substances of a more or less similar chemical nature to oestrone may have some degree of oestrogenic power, even if their primary biological activity is of quite a different nature.³ Further, it has been found possible to hydrogenate oestrone, which itself shows no male hormone activity, to a substance having male hormone activity but no oestrogenic power.⁴ It is not unlikely, therefore, that substances having both male hormone and oestrogenic properties may occur naturally. The first male hormone obtained, androsterone, isolated from male urine by Butenandt⁵ and prepared artificially from cholesterol by Ruzicka and his co-workers,⁶ was found to be non-oestrogenic by the vaginal cornification test⁷ and by a plumage test.⁸ Butenandt and Kudzus,⁹ however, have recently reported that *trans*-dehydroandrosterone, androstenedione, and testosterone cause opening of the vagina in the intact immature rat. The first of these substances is present in human male urine and has some male hormone activity (Butenandt and Dannenbaum).¹⁰ Testosterone, however, isolated from testes by Laqueur and his co-workers,¹¹ is the most active male hormone so far described.

Saturated and Unsaturated Compounds

Butenandt's work provided the first evidence that naturally occurring compounds might show the activities of both ovarian and male hormones. The three compounds found to be oestrogenic by Butenandt are all unsaturated, and therefore more similar to oestrone than is androsterone, but certain saturated compounds of the series, including androstanediol (the dihydroxy derivative of androsterone), are also oestrogenic on the intact immature rat.¹² Moreover, androstanediol increases the size of the uterus and vagina of the adult ovariectomized rat.¹³

Further observations by us confirm and extend these findings. From the table it will be seen that most members of the androsterone-testosterone series cause

Substance	Total Amount given (mg.)	Effect on Vagina of Immature Rat	
		Normal	Ovariectomized
Androsterone	2	— (2)	
Androstanediol	2	+ (1)	
	4	+ (2)	— (1), + (1)
	5		+ (1)
Androstenedione	2	— (2)	
	2.5		— (1)
	3.0	— (1), + (1)	
<i>trans</i> -Dehydroandrosterone	2	+ (2)	— (1) + 1
	3		+ (1)
<i>trans</i> -Androstenediol	2	+ (2)	+ (1)
Methyl <i>trans</i> androstenediol	0.5	+ (2)	
	1.25		+ (1)
	1.5	+ (2)	
	2.0		+ (1)
Methylandrostanediol ...	0.5	+ (2)	
	1.25		— (1)
	1.6		+ (1)
3-Keto-17-methylandrostanol	0.6	+ (2)	— (2)
	1.24		+ (1)
Testosterone	0.125	— (1)	
	0.8	— (1)	
	2.0	— (1)	— (1)
	4.0	— (1)	
	6.0	+ (1)	
Methyltestosterone	0.4	— (1)	
	0.8	— (1)	— (1)
	2.0	— (1)	
	3.0	+ (1)	

Half of the total dose was given on two consecutive days to young female rats 30 to 40 grams weight. + means that the vagina became patent within six days, usually three to four days, after the first injection. Number of animals in each test is given in brackets. In all cases examined histologically opening of the vagina had been accompanied by cornification and by oestrous distension or enlargement of the uterus.

opening and cornification of the vagina and enlargement of the uterus of the immature rat—intact or ovariectomized—in doses comparable with those required to cause detectable growth of the prostate and seminal vesicles of the castrated male rat. The difference in oestrogenic activity between *trans*-dehydroandrosterone and its isomeride testosterone is remarkable. In view of the response of the ovariectomized animal, it is highly improbable that the oestrogenic action is exerted through some other endocrine organ (a similar effect is obtained on adrenalectomized ovariectomized rats, for instance), and the effect is presumably a direct one on the uterus and vagina. Whether or not transformation of the male hormone to oestrone or a similar substance takes place as a preliminary to its acting on the vagina and uterus, is impossible to say at this stage.

Oestrogenic Actions of the Male Hormones

We have also found that *trans*-dehydroandrosterone (1 mg. daily) will cause the appearance of female plumage in the Sebright bantam capon, an effect which can be produced by oestrone but not by androsterone.* (Callow and Parkes.⁹)

In view of these results it seems likely that the oestrogenic action of testis and male urine extracts may be due, at least in part, to the presence of compounds exerting an oestrogenic action in addition to their primary male hormone action, rather than to the actual presence of oestrone or some other purely oestrogenic compound. The importance of this problem has been discussed by Parkes and Zuckerman,¹⁴ and the isolation and identification of the oestrogenic substance or substances of human

* The Sebright bantam cock is hen-feathered, male feathering appearing only after castration. On the basis of their experiment with androsterone and oestrone, Callow and Parkes⁹ were inclined to believe that the hen-feathered condition of the normal male was due to the production of an oestrone-like substance by the testis, but in view of the above result it may equally well be due to the production of one or more of the oestrogenic male hormones.

male urine, if other than *trans*-dehydroandrosterone, would appear to be a matter of pressing importance.

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IMMUNIZATION BY THE ORAL ROUTE IN RESPIRATORY INFECTIONS

WITH SPECIAL REFERENCE TO INFLUENZA, COLDS,
AND THEIR COMPLICATIONS

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Practicability of Oral Route for Vaccination Purposes

In recent years considerable interest has been aroused as to the possibility of utilizing the oral route for prophylactic immunization purposes not only against intestinal infections but against other general infections. There is now definite information on the value of the oral method in prophylactic typhoid immunization. The evidence, based on clinical and serological investigations on man, indicates that the oral method is just as efficient as the subcutaneous method, if not more so. Thus Hoffstadt and Thompson (1929)¹ have shown that agglutinins appear in the blood after three doses of a mixed typhoid and paratyphoid vaccine administered by the oral route on three successive days. They found that of ninety-three persons so treated 88.5 per cent. developed agglutinins for typhoid and a lesser number for paratyphoid bacilli as compared with 80 per cent. who, according to the literature, developed agglutinins after subcutaneous inoculation and 90 to 95 per cent. who show a positive Widal reaction after suffering from the disease. Pijper and Dau (1930)² have also confirmed from the results of their experiments the fact that the oral administration of typhoid vaccine produced agglutinins in man. These were found to be of the O (somatic) variety only. Krause-Shimkin (1931)³ confirmed these results of Pijper and Dau. Ruge (1932)⁴ has recorded a well-controlled experiment of oral vaccination compared with subcutaneous injection. The agglutinins against *B. typhosus* were actually higher in the orally vaccinated group after five