glycaemia, varying from 0.19 to 0.28 per cent., may be found, but the fasting and two-hour blood sugar is always normal. Such variations must depend on varying rates of absorption or other factors which influence a "normal" blood sugar curve to have similar, though minor, variations. Temporary hyperglycaemia and glycosuria is found in these cases not only after a test meal of glucose, but after any meal containing rapidly soluble carbohydrate. It is shortly after such meals that glycosuria is discovered in some routine test.

In several normal individuals the blood sugar curve after glucose by the *mouth* has been compared with the same quantity of glucose injected by tube directly into the *duodenum*. In every case the latter has approximated to the "lag" type by showing a higher and more rapid hyperglycaemia and a quicker return to normal than after oral administration.

There is no evidence in my experience that patients showing this type of blood sugar curve tend to develop true diabetes. In one case glycosuria and "diabetes" were diagnosed in 1913, and in spite of the patient wisely ignoring all diet restrictions, a typical "lag storage" glycosuria was found on repeated examination fourteen years later. I have seen only one patient out of some eighty develop true diabetes, and this might happen by chance, just as diabetes may occasionally develop in a person with renal glycosuria. Such occasional exceptions only prove the rule in negligible glycosuria of these two types.

The Incidence and Explanation of the "Lag Storage" Curve

This paper has been written because of the frequency with which I have observed the condition after gastro-enterostomy. In several cases it was certain that glycosuria was absent before operation. In others, a quickly emptying stomach associated with duodenal ulcer or a very rapid total intestinal transit has been confirmed. In the majority of these curves, however, no symptoms of intestinal abnormalities have been found and have not been looked for by special methods.

The percentage incidence of this curve in the normal population cannot be assessed, but I am sure it is not infrequent. MacLean found that 19 per cent. of cases investigated for symptomless glycosuria fell into this group, while 48 per cent. showed renal glycosuria, and only 21 per cent. diabetic curves. For various reasons I believe that some 5 to 10 per cent. of normal individuals have a low renal threshold for glucose (renal glycosuria), and I think at least 2 per cent. have a "lag" type of curve. Be that as it may, the assessment and recognition of its true meaning is at least of great importance in assurance work.

The explanation of the "lag" is due, in my opinion, entirely to unusually rapid absorption of sugar from the intestine. The storage mechanism of the liver, the muscles, and the tissues cannot deal with the sugar sufficiently quickly, and a brief hyperglycaemia results. In a short time it is fully dealt with, and the glycosuria and hyperglycaemia disappear.

Nomenclature

The name "lag curve" or "lag storage" curve could hardly be worse or more misleading. The name was probably used to suggest that the storage mechanism, the insulin-glycogen storage mechanism in the most widely current view, was delayed in coming into its action. But the curve is the opposite of slow or lagging. It is brief, quick, sharp, and the name "lancet" or "steep" has been suggested. For years I have given it in my notes the title of "oxyhyperglycaemia," which has the double merit of good description and good Greek ($\delta\chi\mu\varsigma$ = sharp, steep). This word falls into line with

several others, such as hyperglycaemia, hypoglycaemia, orthoglycaemia, orthoglycaemic glycosuria (renal glycosuria), oxyhyperglycaemia (glycosuria of "lag" type).

Summary

The "lag" or "lag storage" type of blood sugar curve has been so frequently observed after gastro-enterostomy that its occurrence seems to be due to mere rapid intestinal absorption and not to any defect in carbohydrate metabolism.

The nomenclature of the condition could hardly be more misleading, and a new name, oxyhyperglycaemia, is suggested.

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TESTOSTERONE

BY

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It is now well established that male hormone preparations from testis and from male urine are quantitatively different in their biological action. The clearest distinction is that, per capon unit, testis extracts are much more active on castrated rats than are urine extracts.¹ With the isolation of androsterone, the chief male hormone substance of urine, by Butenandt,² and its artificial preparation from cholesterol by Ruzicka and his co-workers,³ a complete examination of its biological properties became possible. It was then obvious that androsterone could not be the main active principle of testis extracts,⁴ and Ruzicka and Wettstein⁵ suggested that the testis hormone itself might be an unsaturated compound of the same type. In the meantime Laqueur and his co-workers⁶ had isolated from testis extracts a crystalline steroid with a high male hormone activity. Oxidation of this gave rise to a diketone, which was identified as one already "synthesized" by Ruzicka and Wettstein,⁵ and in a very short time the suggestion of the nature of the testis hormone was shown to be correct. Then, in the course of a month or two, the hormone, called testosterone by Laqueur, was produced artificially from cholesterol by Ruzicka and Wettstein⁷ and also by Butenandt and Hanisch,⁸ working independently. So ends an amazing chapter in endocrinological chemistry.

The Androsterone and Testosterone Series

Many other compounds of the androsterone-testosterone series have been prepared artificially,⁹ the majority being more active, but some less active, than androsterone. It is agreed that testosterone is the most active male hormone so far obtained, either naturally or artificially. It is noteworthy that the excreted forms of both the male and the oestrogenic hormones are much less active than the original gonadal forms, while the excreted form of the corpus luteum hormone (pregnandiol) is quite inactive.

According to Laqueur⁶ testosterone is seven times more active on capons than androsterone; Butenandt and Hanisch¹⁰ give the ratio as 6 to 1, Tschopp¹¹ as 8 to 1. In our own experience 16 to 18 gamma of testosterone equals in comb-growth-promoting activity 100 gamma of androsterone (the agreed international unit of male hormone activity). The results correspond very satisfactorily.

Effects on Castrated Animals

It is difficult, if not impossible, to give a definite figure for the activity of testosterone on castrated mammals compared with that of androsterone. Not only are the ratios different for prostate and seminal vesicles, but the slopes of the dose-response curves for the two substances are so different that no ratio is significant unless the level of response at which the comparison is made is also stated. This applies also to other compounds (Parkes).¹² Further, differences in the technique of dissecting and weighing the organs render it difficult even to make the comparison at the same level of response in different laboratories. Tschopp¹¹ states that testosterone given alone is twenty times as active as androsterone on the seminal vesicles. Butenandt¹⁰ finds a ratio of more than 10 to 1. Our own experiments, carried out on groups of five rats castrated at 40-50 grams and used a month later, ten daily injections being given, are summarized in the table. From these results testosterone seems to be about two and a half to five times as active as androsterone on the prostate, the activity varying with the level of response at which the comparison is made. On the seminal vesicles it is about ten times as active at the level of response at which comparison is possible. Tschopp's¹¹ results give much higher ratios than these. Testosterone also differs from androsterone in producing a more normal weight relation between prostate and seminal vesicles.^{4 13}

As regards its activity per capon unit on rats, testosterone does not, in our experience, come up to expectations. Per capon unit it is little, if at all, more active on the prostate than androsterone, whereas testis extracts, per capon unit, are many times more active. In this connexion Laqueur's⁶ statement that the activity of testosterone on rats is greatly enhanced by the simultaneous administration of an α substance, itself inactive, from testis tissue, is of the greatest interest. Ruzicka¹⁴ has recently referred to experiments which seem to confirm this statement.

Methyl and Benzoyl Derivatives

The activity of two derivatives of testosterone has also been investigated: methyltestosterone¹⁴ and testosterone benzoate.¹⁵ The former is produced by the introduction of a methyl group in position 17. Similar treatment of the other compounds of the series increases their activity

Substance	Total Dose (mg.)	Weight of		Amount of Androsterone (mg.) required to give similar effect	
		Prostate (mg.)	Seminal Vesicles (mg.)	On the Prostate	On the Seminal Vesicles
Testosterone	0.6	33	10	3.25	6.0
	2.0	61	27	7.0	20.0
	4.0	96	47	10.0	—*
	6.0	136	84	15.0	—*
	8.0	156	99	—*	—*
Methyl-testosterone	2.0	75	32	9.0	20 +
Uninjected Controls		16	4	—	—

* Glands of this size not obtained in ten days with androsterone.

on rats considerably and their activity on capons slightly. Methyltestosterone proved to be appreciably more active on rats than testosterone (see table), but duplicate tests on capons showed that the activity was considerably less than that of testosterone—only about one-third. As a result, methyltestosterone, per capon unit, is much more active on rats than is testosterone. This is an anomalous result compared with those obtained on the other compounds, and there seems to be no obvious reason for the difference. The behaviour of the benzoate is also peculiar. Androsterone benzoate has a delayed and prolonged action

on the capon comb as compared with androsterone, but the ultimate amount of growth produced by the benzoate is of the same order as that produced by a similar amount of free androsterone. The delay in effect due to benzoylation of androsterone is similar to that produced by benzoylating oestrone, but much more pronounced. Testosterone benzoate, however, even in comparatively "large" doses, has no immediate and little, if any, delayed effect on the capon comb. Thus 1 mg. given over five days to each of a group of five capons produced no detectable enlargement within four weeks. This comparative inactivity of testosterone benzoate is most unfortunate, because the possibility of obtaining a prolonged effect from a short series of injections is of great clinical interest.

We are much indebted to Professor Ruzicka and Messrs. Ciba for supplies of the substances referred to above.

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CHRONIC LEAD POISONING DUE TO THEATRICAL GREASE PAINT

BY

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AND

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We report the following case to draw attention to the possibility of acquiring lead poisoning from the use of theatrical grease paint. This origin for lead poisoning has not previously been recorded so far as we have been able to ascertain. In the patient whose history is set out below, a distinguished actress playing the leading part in a London theatre, a very serious illness resulted from the use of grease paint containing large quantities of lead. The consequences of this illness were disastrous to the patient. She became gravely ill, lost her work, narrowly escaped an abdominal operation, and only began to improve after blood transfusion. Step by step evidence was collected to prove that this was a case of lead poisoning, and finally we were able, by a series of chemical analyses, to trace the poison to its source.

We are informed that grease paint similar to that used by our patient has been offered for sale extensively both in London and the provinces. If this continues other cases of lead poisoning similar to this are likely to occur, as well as much vague ill-health of a less clearly defined nature.

History of Case

The patient was an actress aged 28 years. On January 5th, 1936, she consulted one of us (E. L. B.), saying that she had not felt well for the past four weeks, her symptoms being: