decided that the results were not accurate enough to warrant the use of heparin and dicoumarol in those cases in which the tests were positive.

It was found that there is commonly a fall in coagulation time during or immediately after operation, and it is suggested that thrombosis, if it does occur, probably starts during this period.

I am indebted to Professor Digby Chamberlain, who proposed and guided these investigations, and on whose cases they were carried out.

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INCIDENCE OF SIGNS USUALLY CONNECTED WITH THYROTOXICOSIS WITH SPECIAL REFERENCE TO LID LAG*

BY

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During recent observations on the coincidence of hyperthyroidism and peptic ulcer (Jackson and Pinkerton, 1949) it was noticed that a large proportion of patients with the latter complaint showed von Graefe's sign (lid lag), one of the characteristic ocular phenomena of thyrotoxicosis. This sign was first described in 1864 by von Graefe, who said: "... namentlich folgt bei Senkung der Cornea das obere Augenlid nicht." He remarked that it was not the result of exophthalmos, as it was present in early cases of thyroid disease which showed no proptosis. He considered it to be a sign pathognomonic of hyperthyroidism in the early stage: "... geringen Grade der Krankheit einen pathognomonischen Werth hat." It is now recognized that the sign is not peculiar to thyrotoxicosis (Eason, 1927) and that it may occur in normal people (Joll, 1932). Joll remarks that it also occurs in all forms of goitre, in myotonia congenita, and in all cases of proptosis.

Present Investigation

In order to determine the approximate incidence of lid lag in people without thyroid disease, and to see whether it was particularly common in cases of peptic ulcer, 600 people of all ages and approximately equal sex numbers who attended a general hospital were examined. All patients with dysthyroidism, severe illness, and prolonged pyrexia were excluded. Otherwise there was no selection, except that 38 extra cases of peptic ulcer were specially included. Other manifestations which occur in thyrotoxicosis were also looked for in this series. Preference for hot or cold weather was noted, and the subjects were questioned about excessive sweating. Lid lag, lid retraction, exophthalmos, enlargement of the thyroid gland, and tremor of the outstretched fingers were looked for. The heights and weights of all those over 18 were noted where practicable.

For present purposes lid lag is defined as occurring when a white band of sclera appears between the upper lid and the cornea on following a moving object downwards with the eyes. If lid retraction is present lid lag can be considered to exist only if there is a definite widening of the band of sclera already visible. This is the most objective way of defining lid lag, although in those whose lid is usually held at a low level there may be a degree of lagging

of the upper lid without any sclera coming into view. The results are shown in Table I.

TABLE I.—Results of Investigation

	Total No.	No. with Lid Lag
Whole series	600	85† (14%—or 10% of whole series excluding ulcer cases)
Patients with peptic ulcer	76	23 (33%)
" " lid retraction	14	8 (57%)
" " exophthalmos	3	3 (100%)
" " non-toxic goitre	35	5 (14%)
" " fine tremor	11	

† 58 males, 27 females.

Types of Eyelid Movement.—All cases of lagging of the upper eyelid were not alike. The band of sclera might appear during the whole movement of the eyeball or during any part of it. In other words, the lag might begin as soon as the eyeball started to descend, or the lid might move normally at first and lag later. The movement might be smooth or jerky. The lag in some cases was variable, at times being pronounced and at other times not being elicited at all. In five cases it was unilateral, and in two there was actually a reverse or upward movement of the eyelids as the eyeballs started downward. In one person the lid retraction was unilateral.

Lid Lag in Relation to Other Observations

The male sex predominated in the ratio of 2 to 1. All age groups produced subjects with lid lag, but it was more common in those over 40 (see Table II).

TABLE II.—Age Incidence of Lid Lag

Age	Total No. of Subjects	No. with Lid Lag
0-9 years	31	3 (9.7%)
10-19 "	50	2 (4%)
20-29 "	50	2 (4%)
30-39 "	72	8 (11%)
40-49 "	115	20 (17.4%)
50-59 "	132	22 (16.6%)
60-69 "	107	21 (19.6%)
70-79 "	43	7 (16%)

Eight of the 14 subjects with lid retraction also showed lid lag, as did all three with exophthalmos and five out of the 35 with simple goitres. Of the 76 cases of peptic ulcer 23 (33%) showed lid lag. This incidence is significantly higher than that of lid lag in the control series (10%). The impression was formed that lid lag was more common in thin people, and since peptic ulcer characteristically occurs in people with a low ponderal index (P.I.) (Draper, 1930; Robinson, 1938) this was suspected of being the explanation of the frequent occurrence of lid lag in peptic ulcer subjects. To test this hypothesis the P.I.† of all those over 18 was worked out, and all fell between 1.2 and 3.2. The number of subjects pertaining to each index was noted and expressed as a percentage of the whole. Thus three subjects (0.5% of the total) had a P.I. of 1.3. These percentages for each P.I. referring to (1) all the subjects, (2) the peptic ulcer subjects, and (3) those showing lid lag were plotted separately (see Chart). The mean P.I. in the full control series was 2.1 (slightly in excess of the mode), while in subjects with peptic ulcer and in those showing lid lag it was 1.9. The chart thus confirms the tendency for lid lag to occur in people of slim build, but it seems unlikely that this factor alone can explain its excessive appearance in peptic ulcer subjects. However, the male preponderance in both peptic ulcer—about 4 : 1 (Stewart, 1923; Ryle, 1932; Tidy, 1944 ;

†The ponderal index in this investigation was calculated by dividing the weight in pounds by the height in inches.

*Based on a paper read at the South African Medical Congress, Capetown, September, 1949.

Graph showing percentage of each ponderal index.

Sällström, 1945)—and lid lag—2 : 1 in this series—may also offer a partial explanation.

Other Findings.—The occurrence of 28 cases of greatly enlarged non-toxic thyroid glands in subjects resident in Birmingham puts the approximate rate of simple goitre in this city at 5.6%. It was noted that 125 people preferred cold weather, 273 hot weather, and the remainder were indifferent. All subjects under 20 preferred the heat. Therefore only in young people can preference for cold weather be considered an important diagnostic feature in borderline hyperthyroidism, unless there has been a recent change in preference.

Assertions of excessive sweating were not uncommon, but revealed nothing of particular interest. The very fine rapid tremor generally considered characteristic of hyperthyroidism was found 11 times.

Mechanism of Lid Lag

Von Graefe (1864) believed that the cause of his sign was a disturbance of lid musculature, probably affecting Müller's muscle through the sympathetic system. He observed that morphine abolished the sign. Pochin (1939) believed that the lid retraction (usually combined with lid lag) in Graves's disease was associated with spasm of the levator palpebrae superioris and not with affection of the involuntary muscle. Joll (1932) considered that lid lag was often a "mechanical consequence of forward displacement," but this cannot explain its occurrence in normal people. The observations reported above do little to elucidate the mechanism of the lagging, but suggest that it is more common in thin people.

Summary

The examination of 600 subjects demonstrated the frequency of lid lag, apart from its hyperthyroid connexions. The incidence of certain other signs characteristically occurring in thyrotoxicosis was also estimated in this series. It seems that lid lag is particularly common in people suffering from peptic ulcer, and so cannot be of help in the diagnosis of mild degrees of hyperthyroidism in patients with ulcer.

STATISTICAL NOTE

(1) The male sex preponderance is very highly significant, the difference between proportions being ten times the standard error.

(2) The high incidence of lid lag in peptic ulcer subjects is also significant. The differences between percentages is three times the standard error.

(3) The difference between the mean P.I. of ulcer cases and of the control series and between lid lag cases and controls is over three times the standard error in each instance. The apparent high frequency of lid lag in thin people and in ulcer subjects is thus highly significant.

I should like to thank Mr. Kelman, the medical superintendent, for permission to investigate patients at Selly Oak Hospital.

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ACTINOMYCOTIC EMPYEMA

BY

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Massive empyema due to actinomycosis is uncommon enough to warrant description of a case. Price (1941) states that the empyema is rarely large and the primary lesion seldom pleural. Until recently the prognosis was regarded as unfavourable, death resulting from exhaustion and toxæmia. Penicillin therapy, however, has given promising results in cases cited by Hamilton and Kirkpatrick (1945) and others in this country, and by American authors.

The following case is of interest because a total dosage of over 25,000,000 units of penicillin extending over a period of 56 days was necessary to overcome the infection. Repeated aspirations were necessary owing to the encysted nature of the empyema.

Case History

A carter aged 49 was seen by me in consultation with his own doctor on February 12, 1949. He gave a history of sudden onset of right-sided chest pain and rigors on December 22, 1948. After a few days in bed he resumed his normal activities but did not feel well. On January 29, 1949, the pain returned accompanied by cough and feverishness. His doctor suspected a pleural effusion, but was unable to obtain fluid from the pleural cavity. The temperature was remittent and the dullness increased in spite of treatment with sulphamezathine. The patient had frequent profuse sweats, looked toxic, and had lost weight.

I found him to be moderately dyspnoeic. His pulse rate was 84, regular, and of good volume; respirations, 28; temperature, 101.3° F. (38.5° C.). The apex beat was in the fifth interspace outside the nipple line. His blood pressure was 140/75 mm. Some clubbing of the fingers was present. Examination of the chest showed well-marked signs of a pleural effusion, with stony dullness extending from the base of the right lung to the third interspace posteriorly and forward to the anterior axillary line. B.S., V.F., and V.R. were greatly diminished. There was no bulging of the intercostal spaces. An area of paravertebral dullness was found on the opposite lung. The urine showed no abnormality.

On February 13 he was admitted to the Bolton Royal Infirmary. A radiograph revealed a massive pleural effusion of the right side of the chest, and 10 ml. of thin greenish foul-smelling pus was aspirated and sent to the pathology department. The patient was then put on penicillin, 250,000 units daily in three-hourly injections. On February 24, on receipt