THE EFFECT OF THYROID ADMINISTRATION ON THE BLOOD CHOLESTEROL.

By A. Glen Duncan, M.D., D.P.M.,
Assistant Medical Officer, Severalls Mental Hospital.

In a previous investigation (1) it was ascertained that the amount of cholesterol present in the serum of psychotic patients shows certain variations from the normal, and that it is influenced by the acuteness of the mental condition. Hypercholesterinæmia is usual in all forms of mental disorder except imbecility, and a fall in blood cholesterol content occurs during attacks of excitement, agitation or confusion. These results suggested an association between the blood cholesterol and the nervous system, probably by way of the sympathetic and endocrine gland systems.

The influence of the thyroid was observed during the administration of the dried gland to a sub-thyroidic man whose serum contained the large amount of 502 mgrm. cholesterol per 100 c.c. The mental condition—a profound emotional deterioration—improved practically to normal, and at the same time the serum cholesterol fell to 158. When treatment was suspended it rose to 414, and emotional dullness was again prominent. In view of the simultaneous mental improvement and cholesterol variation effected by thyroid administration, similar treatment was tried in other types of psychosis, and the serum cholesterol estimated at frequent intervals.

The association between thyroid and cholesterol has been noted by other observers, usually as the result of experiments on animals or observations in cases of definite thyroid disease. Luden (2) found the blood cholesterol to be high in myxœdema, with a fall to normal during thyroid treatment. In exophthalmic goitre the figure was within normal limits. Epstein and Lande (3) observed hypocholesterinæmia in Graves's disease and hypercholesterinæmia in cases of subnormal basal metabolism. The results of Laroche (4) were similar. Gardner and Gainsborough (5), using the accurate digitonin method, found the plasma cholesterol in 14 cases of exophthalmic goitre to be lower than the normal average, but practically all within the normal limits of variation. They

concluded that there was no relationship between a raised basal metabolic rate and a low blood cholesterol, but agreed that in untreated cases of myxœdema the plasma cholesterol was high. Wade (6) estimated the blood cholesterol in dogs, and found it to be increased after extirpation of the thyroid and parathyroids. A similar rise occurred after thyroidectomy for exophthalmic goitre and toxic adenoma in man. An increased blood cholesterol in rabbits was also found by Rémond, Colombiès and Bernardbeig (7) after thyroidectomy and parathyroidectomy, and by Onizawa (8) after thyroidectomy. Christie, Lyall and Anderson (9) observed a great diminution under thyroid treatment in a case of xanthomatosis with low basal metabolism and hypercholesterinæmia.

In the present investigation the serum cholesterol was estimated by the colorimetric method, as previously described (1), duplicate extractions being carried out and the mean of the two results taken. The normal limits, ascertained in the former investigation, are taken as 140 and 200 mgrm. per 100 ml. The figures refer to the total of free and combined cholesterol. Blood was obtained by vein puncture between 2½ and 3 hours after breakfast, except in 4 cases, when the blood was taken after 15 hours starvation. Thyroid was administered in the dried gland form.

Twenty-two cases were investigated, all of them male patients in a mental hospital. They included 8 cases of dementia præcox, 4 of melancholia, 1 of mania, 3 imbeciles, 1 confusional case, 1 "insanity with epilepsy," 1 paralysis agitans, 1 post-encephalitic, and 2 general paralytics. The cholesterol variations are indicated in the following notes. The daily amount of thyroid is given as the equivalent of fresh gland. The figure in brackets refers to the day on which each estimation was made, counting from that on which thyroid was commenced.

1. Dementia præcox, sub-thyroidic, æt. 28. Very dull. Resting cholesterol, 502.

During 7 weeks thyroid, 15 gr. daily; after 6 weeks, 158; 7 weeks, 163.

After thyroid: 2 weeks from cessation, 233; 4 months later, 414.

Great improvement during treatment. In this case cholesterol estimations were made in following the mental state, not as a direct study of the effect of thyroid, and were consequently at long intervals.

2. Dementia præcox, æt. 30. Demented; very dull. Resting cholesterol, 227.

During 60 days thyroid, gradually rising to 90 gr. daily: 159 (19th), 149 (39th), 121 (53rd), 119 (60th).

After thyroid: 151 (69th), 186 (74th), 212 (90th), 243 (103rd), 209 (126th), 244 (171st).

No improvement.

3. Dementia præcox, æt. 40. Always more or less stuporose. Resting cholesterol, 246.

During 81 days thyroid, gradually rising to 120 gr. daily: 163 (19th), 148 (39th), 125 (53rd), 116 (60th), 115 (67th), 135 (74th), 122 (81st).

After thyroid: 163 (88th), 209 (95th), 197 (103rd), 243 (114th), 209 (138th), 223 (171st).

Emotional state improved considerably; irritable when on larger doses. Slowly deteriorated afterwards.

4. Dementia præcox, katatonic type, æt. 29. (See Chart 1.)

No improvement.

5. Dementia præcox, æt. 25. Deluded and hostile. Resting cholesterol, 223.

During 45 days thyroid, up to 90 gr. daily: 161 (16th), 135 (23rd), 137 (31st), 127 (38th), 142 (45th).

After thyroid: 158 (52nd), 221 (63rd), 210 (76th), 239 (94th), 250 (125th).

More restless, destructive and hostile during treatment. Great improvement afterwards.

6. Dementia præcox, paranoid type, æt. 33. Very deluded. Resting cholesterol, 253.

During 70 days thyroid, up to 90 gr. daily (11th day), decreased to 60 gr. (34th day), 233 (4th), 202 (11th), 178 (18th), 181 (25th), 188 (32nd), 195 (39th), 181 (47th), 199 (60th), 171 (70th).

After thyroid: 304 (111th).

Became hypomaniacal during treatment; reverted to delusional state afterwards.

7. Dementia præcox, æt. 39. Deluded. Resting cholesterol, 225.

During 16 days thyroid, up to 90 gr. daily: 183 (7th), 164 (16th).

After thyroid: 186 (25th), 225 (35th), 230 (41st), 210 (54th)—hostile, 229 (72nd), 243 (108th).

No mental change.

8. Dementia præcox, æt. 34. Resting cholesterol, 128.

During 16 days thyroid, up to 90 gr. daily: 115 (7th), 92 (16th).

After thyroid: 123 (23rd), 144 (31st), 177 (39th), 163 (52nd), 140 (73rd), 172 (105th).

No mental change.

9. Chronic melancholia, æt. 36. Depressed and self-absorbed. Resting cholesterol, 341.

During 17 days thyroid, up to 80 gr. daily: 243 (17th—agitated).

After thyroid: 334 (38th), 344 (67th), 374 (115th).

Became agitated during treatment.

10. Melancholia, chronic nephritis, æt. 54. Depressed, self-absorbed. Resting cholesterol 335.

During 37 days thyroid, up to 90 gr. daily: 176 (8th), 195 (15th), 187 (23rd), 231 (30th), 232 (37th).

After thyroid: 232 (44th), 468 (55th), 432 (65th), 552 (86th), 573 (117th).

Between the 23rd and 30th days the amount of thyroid taken is doubtful, as the patient hid some of the tablets in his mouth and subsequently removed them.

No improvement during treatment; more self-absorbed afterwards.

11. Melancholia, senile, æt. 70. Arterio-sclerosis. Resting cholesterol, 242.

During 27 days thyroid, up to 90 gr. daily: 189 (6th), 187 (13th), 166 (20th), 143 (27th).

After thyroid: 184 (34th), 260 (41st), 273 (48th), 263 (62nd), 256 (77th), 287 (119th).

Blood taken while patient fasting. No mental change.

12. Melancholia, æt. 42. Syphilitic. Depressed, mildly agitated, hypochondriacal. (See Chart 2.)

No mental change.

13. Recurrent mania, æt. 43. Exalted; grandiose delusions. (See Chart 3.)

No change during treatment. Improvement afterwards, with a temporary relapse.

14. Confusion, chronic nephritis, æt. 38. Resting cholesterol, 233.

During 13 days thyroid, up to 60 gr. daily: 174 (6th), 135 (13th).

After thyroid: 176 (20th).

Blood taken with patient fasting. No improvement.

15. General paralysis, æt. 54. Demented. Resting cholesterol, 189.

During 14 days thyroid, up to 90 gr. daily: 144 (7th), 116 (14th).

After thyroid: 136 (21st), 203 (35th), 205 (42nd), 242 (56th), 202 (71st), 233 (113th).

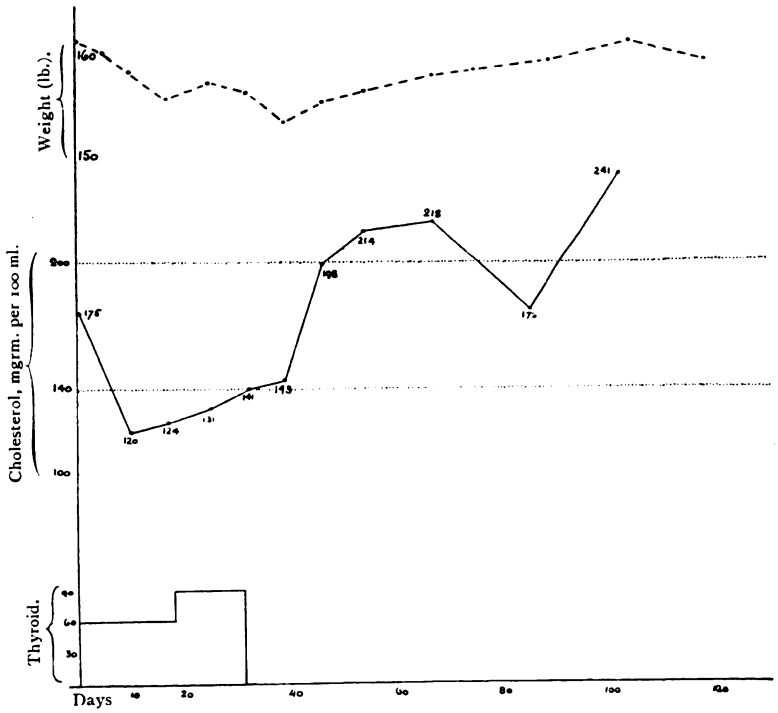

CHART 1.—Dementia præcox.
The dotted lines represent the normal limits of serum cholesterol.

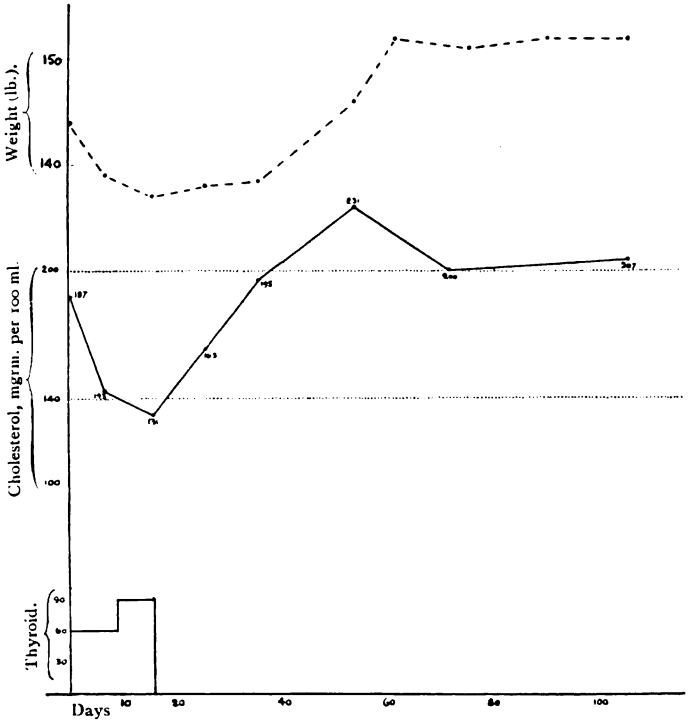

CHART 2.—Melancholia.

https://doi.org/10.1192/bjp.77.317.332 Published online by Cambridge University Press

Less amenable and more difficult to nurse during treatment. Blood taken while patient fasting.

16. General paralysis, æt. 40. Demented. (See Chart 4.)

Had a seizure while on thyroid; more irritable. Improved later and was discharged.

17. Secondary dementia, paralysis agitans, æt. 53. Resting cholesterol, 149.

During 14 days thyroid, up to 90 gr. daily: 100 (7th), 90 (14th).

After thyroid: 97 (21st), 160 (28th), 205 (35th), 212 (42nd), 190 (56th), 171 (71st), 175 (113th).

Blood taken with patient fasting. More tremulous during treatment.

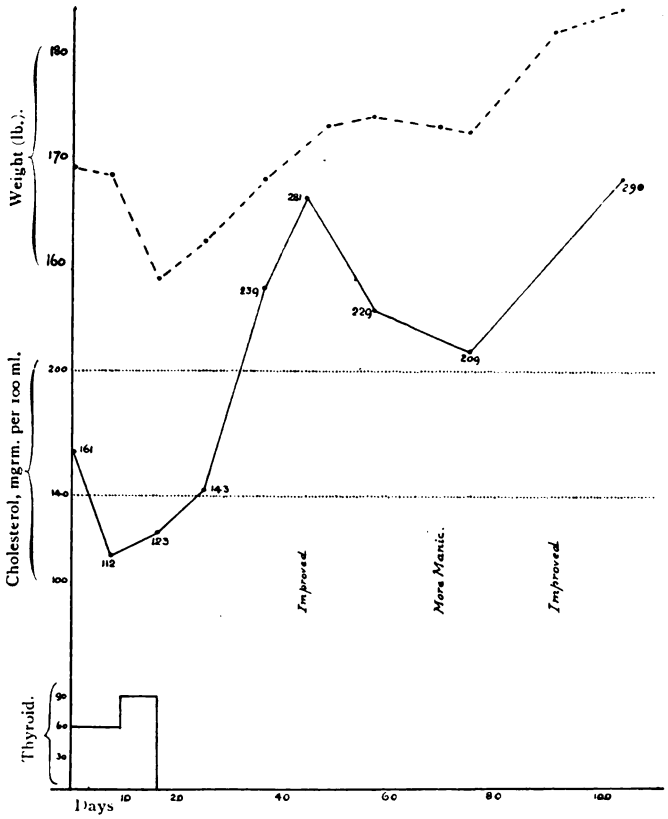

CHART 3.—Mania.

18. Secondary dementia, post-encephalitic, æt. 20. (See Chart 5.)

Signs of thyroidism on 7th day. No change in mental state.

19. Epilepsy, æt. 64. Demented. Resting cholesterol, 201.

During 14 days thyroid, up to 90 gr. daily: 154 (7th), 121 (14th).

After thyroid: 137 (21st), 210 (29th), 229 (37th), 208 (50th), 218 (71st), 202 (103rd).

No mental change.

20. Imbecile, deaf-mute, æt. 41. Resting cholesterol, 152.

During 16 days thyroid, up to 90 gr. daily: 138 (7th), 131 (16th).

After thyroid: 152 (25th), 220 (35th), 214 (41st), 209 (54th), 229 (72nd), 238 (108th).

No mental change.

https://doi.org/10.1192/bjp.77.317.332 Published online by Cambridge University Press

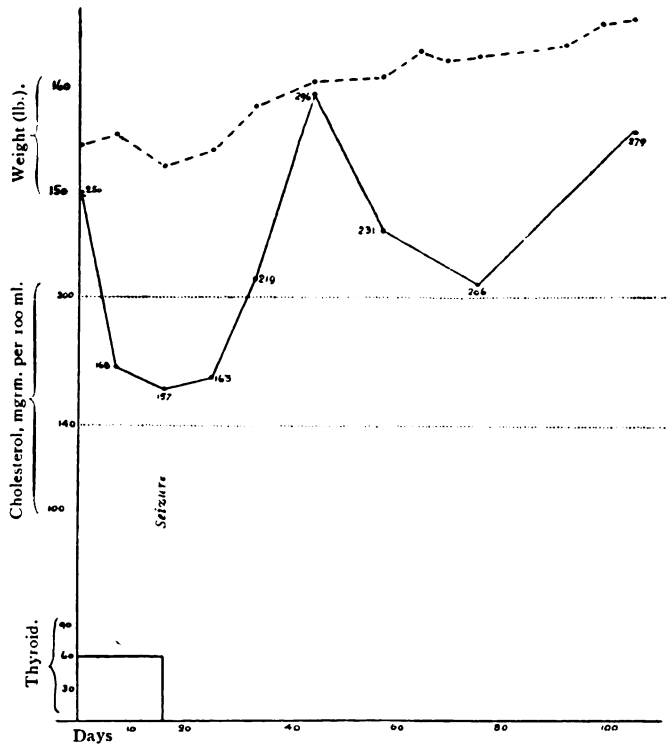

CHART 4.—General paralysis.

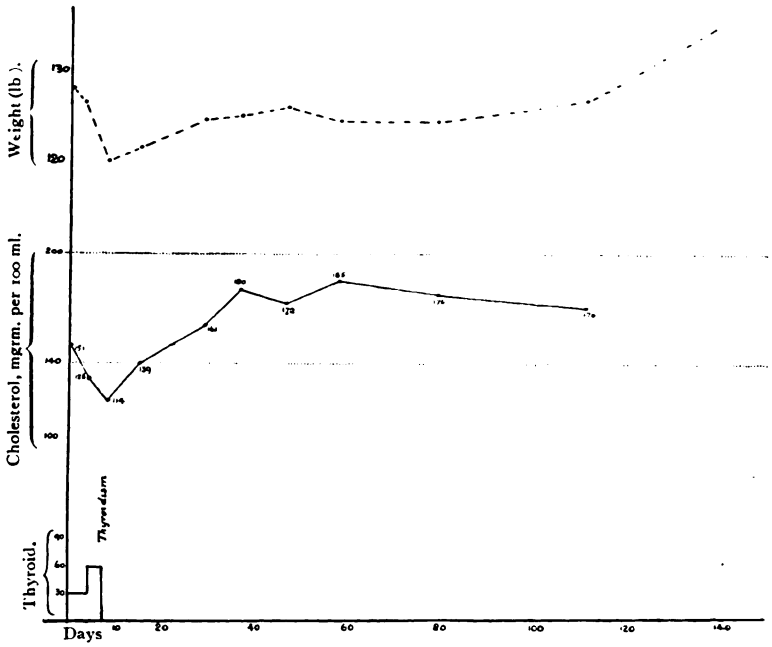

CHART 5.—Post-encephalitis.

https://doi.org/10.1192/bjp.77.317.332 Published online by Cambridge University Press

21. Imbecile, epileptic, æt. 45. Frequent minor seizures and almost incessant muscular twitchings. Resting cholesterol, 103.

During 21 days thyroid, 30 gr. daily: 136 (4th), 87 (9th), 87 (14th), 104 (21st).
After thyroid: 130 (28th), 128 (43rd), 117 (85th).
No improvement.

22. Imbecile, hydrocephalic, æt. 49. (See Chart 6.)
No mental change.

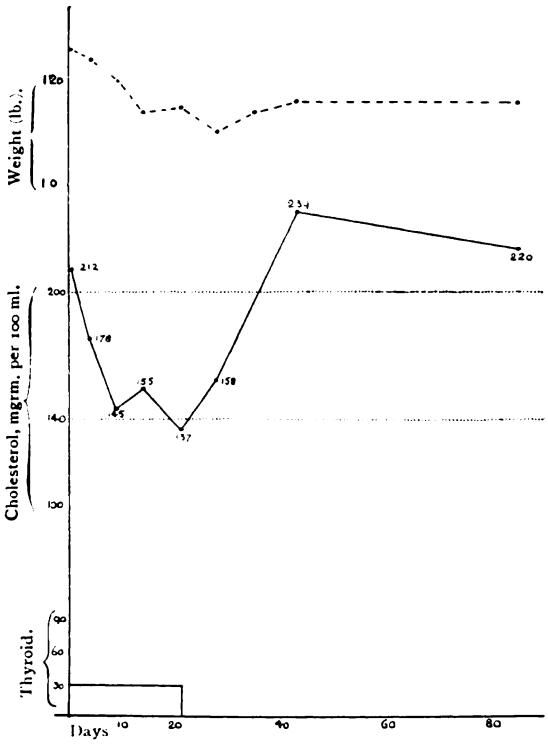

CHART 6.—Imbecile.

It is apparent from the above results that thyroid administration causes a rapid lowering of blood cholesterol. A small dose—the equivalent of 30 gr. of fresh gland daily—is sufficient to effect this; with larger doses the fall is greater and more rapid. After a week or ten days diminution is more gradual, or the amount may remain practically unchanged, or even increase. The effect of increasing the thyroid dosage at this stage is usually a further gradual cholesterol diminution, but even with large doses—equal to 90 or 120 gr. of fresh gland daily—there may be a steady slight rise in serum cholesterol. The result of stopping the thyroid administration is a rise in the cholesterol content, less rapid than

the original fall, but usually reaching a figure considerably above the former resting value.

This variation is not dependent on an initial hypercholesterinæmia, but it is most marked when the resting cholesterol is high. A moderate degree of hypercholesterinæmia is easily reduced to an abnormally low amount by thyroid. The maximum variation was found in Case 10—chronic nephritis with melancholia—a fall from 335 to 176 being followed by a rise to 573. The lowest value induced by thyroid treatment was 87 (Case 21) in an epileptic imbecile whose serum cholesterol was invariably below the normal limits, probably as the result of numerous minor seizures. This was also the only case in which an initial rise in cholesterol was observed, the preliminary figure probably being low as the result of the epileptic attacks.

The subjects of this investigation were patients suffering from a wide variety of mental disorder, including psychoses and congenital defects, "functional" and organic. Considering the constancy of the reaction of the serum cholesterol to thyroid in these, it is reasonable to assume that the effect of thyroid is not confined to psychotics and imbeciles, but also occurs in the normal individual. It has not been possible to carry out a complete test on a healthy man, but one to whom a small dose was given for a week showed a fall of serum cholesterol from 165 to 150; there was no opportunity for further estimations.

The existence of this reaction makes it possible to suggest an explanation for the high blood cholesterol often observed in psychotics and for the temporary decrease associated with an acute emotional state such as excitement or agitation. Imbeciles, who generally have a blood cholesterol value within normal limits (unless epilepsy is a complication) are detained in a mental hospital principally on intellectual grounds; emotional changes are not common or severe. Psychotics, whatever the variety of the disorder, very commonly have some emotional abnormality. A large group, including many primary dements, are apathetic; many others—the epileptics, mood-psychotics and some alcoholics—are unstable, and subject to severe emotional disturbances; a small minority, including some secondary dements and chronic delusional states, though emotionally stable, have usually passed through a phase of fear, anger, hostility or exaltation. There is some evidence for regarding the thyroid secretion as part of the mechanism concerned with the bodily reaction to an emergency, including the emotional changes of this reaction. From the disuse of this

mechanism there will result the hypercholesterinæmia seen in states of sub-thyroidism and of emotional deterioration. Its temporary working causes the lowering of blood cholesterol observed in states of excitement, agitation and hostility, similar to that obtained by thyroid administration. Periodic excessive use is the possible cause of hypercholesterinæmia in the insane, other than the apathetic group; a temporary diminution is followed by a rise to an abnormal degree, the prolonged emotional reaction or its frequent repetition resulting in persistence of blood cholesterol at a high level.

Although the object of this article is to record cholesterol variations rather than clinical changes, these are summarized for the sake of completeness. In 3 of the 8 dementia præcox cases a definite improvement coincided with the diminution of serum cholesterol; 2 of these who were extremely dull, brightened considerably under treatment, and became apathetic after its suspension; the third, a very deluded man, full of bitter complaints lost his delusions and became mildly hypomaniacal, remarkably pleased with himself and all around him; he also returned to his former state when thyroid was stopped. One dementia præcox patient became worse and was more hostile. In one melancholia case increased agitation was the result. The one maniacal patient remained so until about three weeks after cessation of thyroid, when considerable improvement coincided with a great increase of blood cholesterol. The remaining patients showed no mental change, except that both general paralytics (chronic cases, improved to a stationary condition after malaria) became less amenable and more difficult to nurse. The man with a post-encephalitic condition soon showed signs of thyroidism, and in the case of paralysis agitans the tremor was increased. Evidently any change accompanying thyroidic diminution of blood cholesterol will result from the increased excitability of the nervous system.

I have to thank Dr. R. C. Turnbull for permission to publish these notes.

References.—(1) Duncan, *Journ. Ment. Sci.*, 1930. (2) Luden, *Mayo Clinic Papers*, 1918.—(3) Epstein and Lande, *Arch Int. Med.*, 1922.—(4) Laroche, *Presse Méd.*, 1929.—(5) Gardner and Gainsborough, *Brit. Med. Journ.*, 1928.—(6) Wade, *Amer. Journ. of Med. Sci.*, 1929.—(7) Rémond, Colombiès and Bernardbeig, *Compt. Rend. Soc. Biol.*, 1924.—(8) Onizawa, *Journ. of Biochem.*, 1929.—(9) Christie, Lyall and Anderson, *Brit. Journ. of Derm. and Syph.*, 1930.