patients they occurred at as low a level as 32 mg./100 ml., and other patients were symptom-free at levels of 40 to 45 mg./100 ml.

The outstanding feature about these results was the complete absence of deafness or tinnitus in every patient during treatment with ortho-cresotinate.

Body Weight.—Weight changes during the control period ranged from a gain of 0.7 kg. to a loss of 3.7 kg. During treatment with ortho-cresotinate two patients showed a slight increase in weight and the others lost from 0.4 to 4.6 kg. It was the patient whose diet was reduced from 287 to 200 g. of carbohydrate daily who lost 4.6 kg.

Discussion

These results show that ortho-cresotinate has a similar hypoglycaemic action to aspirin in diabetes mellitus. A disadvantage of aspirin therapy in diabetes mellitus is the fairly frequent occurrence of side-effects with the high dose of the drug required to cause a maximum hypoglycaemic effect. The annoying symptoms of deafness and tinnitus often occur during treatment with aspirin, but neither of these symptoms was experienced by any of the patients treated with ortho-cresotinate.

The drug was given with the aim of attaining a serum cresotinate level of 30 to 40 mg./100 ml. and the serum levels during the course were in the range of 27 to 40 mg./100 ml. for individual patients. With these doses there was a high incidence of temporary side-effects from the drug, the most common being headache (3 patients), anorexia (4 patients), nausea (5 patients), vomiting (3 patients), dizziness (3 patients, and drowsiness (1 patient). These side-effects were due to overdosage, and their occurrence indicates that ortho-cresotinate therapy, like aspirin, requires to be controlled initially by estimations of serum level of the drug until a suitable dose has been determined for each patient. This is necessary because of the variation in the dose required by individual patients to attain the same serum level of the drug. This means that it is advisable to admit patients to hospital to start ortho-cresotinate therapy until the precise dose for each individual has been determined. A slow build-up of dose is recommended to prevent the development of undesirable side-effects.

Summary

The effect of ortho-cresotinate in diabetes mellitus has been investigated in nine patients by administering the drug for two to three weeks after an initial control period. In the six patients previously treated by diet alone a course of ortho-cresotinate relieved mild symptoms of diabetes and caused a fall in fasting blood-sugar and a reduction in glycosuria in all cases. During a course of the drug in the other three patients already being treated with insulin the insulin requirement of all three patients was reduced and in one patient 28 units of insulin zinc suspension daily was replaced by ortho-cresotinate therapy with satisfactory control of the diabetes.

No deafness or tinnitus was experienced by any of the patients, and the most frequent side-effects which occurred in seven patients were headache, anorexia, nausea, and vomiting. These were all temporary, and could be avoided by slowly increasing the dose until the required amounts for each individual patient had been reached.

Ortho-cresotinate has a similar hypoglycaemic effect to aspirin in patients with mild to moderately severe diabetes mellitus without the undesirable side-effects of deafness and tinnitus.

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REFERENCES

- Benedict, S. R. (1911). *J. biol. Chem.*, **9**, 57.
Greenberg, L. A., and Lester, D. (1944). *Ibid.*, **154**, 177.
Lehmann, H., and Silk, E. (1952). *Biochem. J.*, **50**, xxxi.
Reid, J., Macdougall, A. I., and Andrews, M. M. (1957). *Brit. med. J.*, **2**, 107.
Stockman, R. (1912). *J. Pharmacol. exp. Ther.*, **4**, 98.
Trinder, P. (1954). *Biochem. J.*, **57**, 301.

TWO TYPES OF LUPUS ERYTHEMATOSUS CELL FACTOR, SHOWN BY INDUCED L.E. CELL PHENOMENON IN DOGS

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In a previous paper (Bencze, 1960) it was shown that typical lupus erythematosus (L.E.) cell formation can be induced in dogs by transfusion of systemic lupus erythematosus (S.L.E.) plasma. Similar investigations completed on hospital patients gave evidence of the existence of transferable and non-transferable L.E. plasma factors (Bencze, Kovács, and Cserhádi, 1959).

The present communication reports on two types of L.E. plasma factor, as shown by the results of transfusing S.L.E. plasma in experiments on dogs. The experiments were done according to the technique described previously (Bencze, 1960).

Results

The plasma containing L.E. cells from nine patients with typical signs of S.L.E. was transfused into 17 dogs (Table I). The introduction of plasma from three S.L.E. patients produced the L.E. cell phenomenon in the dogs. On the other hand, plasma from six S.L.E. subjects failed to induce the L.E. cell phenomenon.

Further human and animal experiments were carried out with plasma containing L.E. cells from 11 donors (Table II). Plasma of six S.L.E. patients was transfused into human subjects as well as into dogs; plasma from five S.L.E. donors was transfused either into human subjects or dogs, but not both. The plasma from six S.L.E. patients gave identical results in man and dog. The transferable L.E. cell factor produced the L.E. cell phenomenon both in man and in dog (Table II, lines 1 and 2). In four cases the L.E. plasma factors proved

[illegible]

Summary

Two types of L.E. cell factors—transferable and non-transferable—were found in experiments in which plasma from patients with systemic lupus erythematosus was transfused into dogs.

Identical results were obtained in human subjects and in dogs with transfusions of transferable and non-transferable L.E. plasma factor.

The amount of transfused L.E. plasma appears not to be responsible for the production of two types of L.E. cell factor.

REFERENCES

- Bencze, G., Kovács, J., and Cserháti, I. (1959). *Brit. med. J.*, 2, 864.
— and Ludányi, M. (1960). *Ann. rheum. Dis.*, 19, 48.

IS THERE A STEIN-LEVENTHAL SYNDROME?

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During the past twenty years much attention has been paid to the pathological findings in cases of multiple small cysts in ovaries with thickened capsules. Stein and Leventhal (1935) first described a group of cases with such findings and have recently reiterated their conception of what has become known as the Stein-Leventhal syndrome. Stein (1959) defines it as "sterility accompanied by secondary amenorrhoea, hirsuties in 50–75%, and consistently enlarged symmetrical ovaries with a definite pathological pattern." The ovarian changes, he says, may also be found in cases of the adrenogenital syndrome. Leventhal (1958) describes the ovarian pathological findings. The tunica is thick, tough, and pearly white. There are multiple small cysts. The follicles may or may not have layers of granulosa cells. The most consistent finding he describes is hyperplasia of the theca interna with frequent luteinization. The absence of corpora lutea or corpus luteum cysts is noted, and he states that when secretory endometrium is found there is again no evidence of corpora lutea, but marked luteinization of the theca.

Present Investigation

The findings at Chelsea Hospital for Women have been quite different from any reported so far, and are therefore worthy of note.

The clinical features are correlated with the histological findings in two groups, while a third group acts as a control.

Group 1: Typical histology + clinical syndrome of infertility, irregular periods, and hirsutism.

Group 2: Typical histology + clinical syndrome and corpus luteum.

Group 3: Controls; patients in the same age-group, seen during the same period of time, but with varying indications for operation.

The main findings, histologically, are recorded in Table I. All the histological preparations which provide the material for this analysis were examined "blind," and no indication was given of the group to which the section belonged. It will be noted that histological changes in the ovarian capsule are not included in the table, and this is because we have not found it possible to decide a "normal" for each age, owing to the wide variation in the thickness of the capsule. The clinical features are recorded in Table II.

It will be seen that our findings approximate fairly closely as regards the large number of cystic follicles, while the operation notes mention the tough fibrous capsule. A layer of granulosa cells is present in all but one of our cases, but hyperplasia of the theca interna is not as evident as Leventhal has found. In fact, though the theca interna has been present, hyperplasia has not been noted in a single case (Table I).

Luteinization of the theca interna has not been a feature in the cases studied, though it is thought by Shippel (1955) and by Plate (1958) to constitute the principal finding. This hyperthecosis is reported as affecting the theca externa as well, but in our series no cases have come to light where the theca externa has shown hyperplasia. Leclercq (1958) in a series of 51 cases reports very similar findings to those of Leventhal, but we are unable to find the same degree of specificity described by them.

Ovulation has been reported by Stein *et al.* (1949) as occurring very rarely, at long intervals, or not at all; and Kaufman *et al.* (1959) refer to a characteristic lack of recent corpora lutea. Shippel mentions ovulation as a freak occurrence; Ingersoll (1955) says that all the patients are anovulatory, the only common finding being the ovarian pathology; while Prunty *et al.* (1958) also note the absence of ovulation in this syndrome. Bailey (1959) found no corpus luteum in 63 cases. The striking thing about our cases is the comparatively large number showing corpora lutea.

The question of ovulation is obviously of prime importance, since the object of treating these patients is to enable them to ovulate and thus become pregnant. The operation of wedge resection, detailed by Leventhal (1958), may produce regular menstruation in a patient who was previously ovulating with an irregular cycle. It is doubtful whether the operation is indicated in such cases.

Wedge resection may also produce normal ovulatory cycles in patients who were previously suffering from amenorrhoea. The continuance of normal cycles, with or without ovulation, is not necessarily permanent after the operation (Table II).

Groups 1 and 2 show the same features except for the evidence of recent ovulation in group 2. It will also be seen that there is no typical histological pattern of the ovaries which serves to distinguish either of these groups from the controls.

Hirsuties was considerable in three cases in group 1 while the other four showed slight excess of hair. In group 2 (patients who were ovulating) there was considerable hirsutism in four, and two showed a slight excess of hair. The other case in this group was interesting, because, though there was hirsuties of the face and trunk, the hair on her head was absent and she needed to wear a wig. Hirsuties was present in one case in the control group.