are included in the section headed "ancillary investigations." Only results relevant to a diagnosis of thyrotoxicosis are shown in this column.

Of the 26 cases, 25 showed a shortened circulation time, the curious exception (Case 22) having a psychosis (agitated depression) necessitating certification some two weeks post-operatively.

In eight cases the circulation time was re-estimated after apparent restoration to euthyroidism following medical or surgical treatment. In two cases a hyperdynamic circulation persisted—one six months after partial thyroidectomy and another after 22 months' thiouracil treatment.

First Control Series

Table II shows details of 14 cases with thyroid enlargement and associated symptoms, or with persistent symptoms following partial thyroidectomy for thyrotoxicosis. All were clinically adjudged euthyroid. In Cases 7, 8, and 14, thyroidectomy was subsequently performed—one for retrosternal extension and two for tracheal compression. In one case (No. 1) cautious medical treatment was undertaken, in deference to a raised B.M.R. reading, associated with a past history of partial thyroidectomy. It is noteworthy that no case in this group had vascular bruit over the thyroid gland. All members of this group had normal circulation times.

Second Control Series

Table III shows some details of 20 patients in whom a psychiatric diagnosis was eventually established. None had thyroid enlargement, and in no instance was a diagnosis of

TABLE III.—*Second Control Series*

Case	Sex	Age	Clinical Features	Circulation Time (Foot-arm)	Remarks
1	F	54	Agitated depression	20 secs.	Marked improvement on E.C.T.
2	M	40	Cardiac neurosis	8 "	B.M.R. +6. Improved on sedation and reassurance
3	M	25	Hysterical hyperpnoea. Early schizophrenia	6 "	Transferred to psychiatric hospital
4	F	47	Menopause. Cardiac neurosis	11 "	B.M.R. -2. Improved on sedation and reassurance
5	F	18	Hysterical hyperpnoea	10 "	Recovery on sedation and psychotherapy
6	M	28	Acute anxiety. Attacks of tachycardia and sweating	9 "	B.M.R. +5. Improved after sedation, cardiac investigation, and reassurance

Cases 7 to 20 were out-patients with acute anxiety state. All of these showed "foot-minus-arm" circulation times within a range of 9 to 17 seconds.

thyrotoxicosis made on clinical grounds. All were followed up for short periods of up to three months. Most of these were cases of acute anxiety state in whom dyspnoea, tachycardia, or loss of weight featured prominently. For obvious reasons it was not desirable to admit all cases to hospital for detailed investigation.

The circulation time was within, or above, the normal range in 19 instances, the only case with a hyperdynamic circulation (No. 3) having a psychosis.

Discussion

Several causes of hyperkinetic circulation are now recognized, and it is therefore necessary to exclude them before a shortening of circulation time can fairly be attributed to thyrotoxicosis. These causes include pregnancy, anaemia, aortic incompetence, Paget's disease of bone, advanced hepatic failure, arteriovenous aneurysm, beriberi. These conditions are easily separated from thyrotoxicosis, and their exclusion rarely creates a problem, with the possible exception of vitamin-B deficiency.

Williams *et al.* (1943) found biochemical evidence of thiamine deficiency in 75% of a group of 40 unselected

thyrotoxic subjects, and regarded this as being due to a combination of increased requirement and excretion of thiamine.

Since Wenckebach (1934) and other investigators have demonstrated a hyperkinetic circulation in beriberi, it is possible that vitamin-B deficiency of subclinical degree may be a factor in the circulatory acceleration of thyrotoxic subjects. This may explain some discrepancies in either degree or duration of hyperkinesis, but does not affect the first finding of this investigation—that virtually all thyrotoxic subjects have some degree of circulatory acceleration.

The second finding is that psychogenic disturbances, under amylobarbitone sedation, do not result in hyperkinesis. Thus a relatively simple test can be used to resolve the differential diagnosis of thyrotoxicosis and uncomplicated anxiety state.

Summary

The circulation time, calculated by the method described, is considered to be a valuable ancillary investigation in the diagnosis of thyrotoxicosis, provided other causes of hyperdynamic circulation are recognized and excluded.

The method used is regarded as safe and easy; in several instances it was performed on out-patients.

In a group of 26 thyrotoxic cases, 25 had a circulation time below normal limits.

In a group of 20 psychiatric cases, only one case had a shortened circulation time.

In a group of 14 euthyroid patients with thyroid enlargement, all cases had normal circulation times.

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TREATMENT WITH INSULIN ZINC SUSPENSIONS

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Further evidence regarding the results of insulin zinc suspension therapy is provided by the series of 52 patients reported here. Treatment was given in the wards in 36 of these cases, the remainder being treated throughout as out-patients. This trial has been in progress for the past nine months.

Results were classified as good if the fasting, noon, and evening blood sugars (estimated by King's method) were within normal limits, such results being confirmed by further satisfactory urine and blood-sugar tests.

The quantity of carbohydrate in the diets varied from 140 to 250 g. a day, generally divided into approximately equal rations at the four main meals, with snacks at mid-morning and bedtime. In some cases in which the noon blood sugars remained high as compared with those later in the day, the carbohydrate was reduced at breakfast, more being given at lunch and/or the later meals.

Results

The results are summarized in Table I. In the whole series good control with insulin zinc suspension (I.Z.S.) alone was obtained in 42 patients, 16 of whom had had no previous insulin treatment. Four other patients were reasonably well controlled with I.Z.S. mixtures, two requiring the

TABLE I.—Summary of Results of Treatment of 52 Patients with Insulin Zinc Suspensions

Previous Insulin Therapy	No. of Cases	Type of Insulin Zinc Suspension	Results of Treatment	
			Good	Poor
None ..	16	I.Z.S.	16	—
S.I. b.d. {	9	I.Z.S.	7	2
	3	I.Z.S. + I.Z.S.A.	2	1
S.I. + P.Z.I. {	18	I.Z.S.	15	3
	2	I.Z.S. + I.Z.S.C.	2	—
P.Z.I. ..	1	I.Z.S.	1	—
G.I. ..	3	I.Z.S.	3	—

S.I.: Soluble insulin. P.Z.I.: Protamine-zinc insulin. G.I.: Globin insulin. I.Z.S.: Insulin zinc suspension. I.Z.S.A.: Insulin zinc suspension (amorphous). I.Z.S.C.: Insulin zinc suspension (crystalline).

further addition of the "amorphous" preparation and two the addition of the "crystalline" preparation to the I.Z.S. The doses required for stabilization exceeded 50 units in nine patients. Seven of the successfully treated patients showed improved control over that obtained with previous insulin therapy.

The six cases not successfully controlled by I.Z.S. (Table II) had previously been on older insulin therapy, although two of them had not been well controlled just before starting I.Z.S. There was rapid worsening of the diabetic state

TABLE II.—Data of 6 Cases Showing Poor Response to Insulin Zinc Suspensions Following Transfer from Older Insulins

Case No.	Previous Insulin (Units)	Blood Sugars			Insulin Zinc Suspension (Units)	Blood Sugars		
		F	N	E		F	N	E
1	S.I. b.d. 24 + 12	156	82	177	I.Z.S. 60	446	364	275
2	S.I. b.d. 38 + 26	184	106	158	I.Z.S. 72	235	336	206
3	S.I. b.d. 28 + 12	122	85	107	I.Z.S. 44	332	495	535
					I.Z.S.A. 24 + I.Z.S.C. 30	140	136	296
4	S.I. 24 + P.Z.I. 20	172	120	96	I.Z.S. 56	342	394	136
5	S.I. 30 + P.Z.I. 24	256	147	215	I.Z.S. 76	294	403	203
6	S.I. 14 + P.Z.I. 18	400	272	206	I.Z.S. 40	240	360	496

F = Fasting. N = Noon. E = Evening.

in some of these patients, particularly in Cases 1, 2, and 3, which had been well controlled on two daily injections of soluble insulin. Because of this and the time which would have been needed for further experimenting with I.Z.S. mixtures, it was found necessary to return these patients to their older insulin therapy.

Hypoglycaemic Reactions.—These were marked in only two patients, despite the occasional finding of low blood sugars in others.

Local Reactions.—Only one patient showed local inflammatory reactions at the sites of injection for several weeks. One other patient developed insulin atrophy of the abdominal wall, which he had been using exclusively for his injections.

Discussion

In view of the high proportion of successes with I.Z.S. recorded here and by other observers, it is justifiable to try this preparation in all new cases requiring insulin therapy, unless the presence of a severe infection or marked ketosis makes initial treatment with soluble insulin advisable. The marked infrequency of local reactions confirms the view that I.Z.S. should be used in those patients developing local sensitivity with the older insulins.

A high percentage of patients on two daily injections of soluble insulin or on injections of P.Z.I. and S.I. mixtures

can be stabilized on I.Z.S., as has been demonstrated in this series. Nevertheless, in some patients such transfer is attended by the risk of a temporary and sometimes marked deterioration of the diabetic state, as has been noted above (see Table II), and similar instances have been recorded by Fitzgerald *et al.* (1954). Oakley (1953) noted poor control on I.Z.S. in some of his patients transferred from the older insulins. This risk can be reduced by making the change gradually if the total daily dose of the older insulins is a large one, this procedure entailing the separate injection of the older and newer insulins during the period of transfer. There is obviously a strong case to be made for a trial with the insulin zinc suspensions in patients on two daily injections of the older insulins, but patients well balanced on one daily injection of the older insulins could justifiably be left alone, bearing in mind the possibility of difficulties arising after transfer to I.Z.S. On the whole I believe that patients passing through a difficult phase on soluble insulin or soluble and protamine-zinc insulin mixtures should have control restored by increasing the dose of these insulins before attempting transfer to I.Z.S.

Comparison with globin insulin is difficult because of limited experience. The three patients in this series transferred from globin insulin to I.Z.S. were well controlled by the latter, two of them much better than they had been on globin insulin, but the reverse effect was noted by Murray and Wilson (1953) and Fitzgerald *et al.* in each of their cases.

Hallas-Møller *et al.* (1952) stated that patients difficult to control on I.Z.S. alone can generally be stabilized on mixtures of two of the three suspensions. Nabarro and Stowers (1953) found that some of their patients needed a higher proportion of I.Z.S. (crystalline) in the mixture. On the other hand, the type of case normally controlled by an S.I./P.Z.I. mixture of 2:1 or higher may well need more I.Z.S. (amorphous). In this series, four patients not well controlled by I.Z.S. alone were reasonably well stabilized by I.Z.S. mixtures. A small percentage of severe diabetics are best controlled on two or more daily injections of soluble insulin.

Summary

A series of 52 cases of diabetes mellitus were treated with insulin zinc suspension. All 16 new cases were satisfactorily stabilized on this preparation. Of the 36 patients transferred from treatment with older insulins, 26 were satisfactorily controlled by I.Z.S. alone, and 4 other cases reasonably well controlled by I.Z.S. mixtures. Six patients were restored to their previous insulin treatment because it had been more effective, and in some of them the diabetes had become markedly out of control whilst on I.Z.S.

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The National Association for the Prevention of Tuberculosis has published a revised edition of *Help for the Tuberculous* (68 pages). It gives particulars of facilities available for tuberculous patients under the National Health Service and explains the provisions for the medico-social care of patients and their families. Sections on rehabilitation and future development in this field are also included. The booklet is published by the N.A.P.T. at Tavistock House North, Tavistock Square, London, W.C.1, price 5s.