woman, six months postpartum, who gave a history suggestive of progressive hypopituitarism and died of adrenocortical insufficiency after appendicectomy. They also found that the thyroid showed Hashimoto's disease. No mention was made of the stomach, and the adrenals could not be found at necropsy. In neither case are the histological changes in the pituitary those seen in healed postpartum necrosis (Sheehan and Summers, 1949) or in giant-cell granuloma of the pituitary (Oelbaum and Wainwright, 1950 ; Doniach and Wright, 1951).

The adrenals in the present case show the features secondary to prolonged hypopituitarism. Though no Askanazy cells or lymphoid follicles with active germinal centres are present in the thyroid, the acinar atrophy with fibrosis and lymphocytic infiltration is now regarded as being sufficient for the diagnosis of focal lymphocytic thyroiditis. This is believed to be a focal form of Hashimoto's disease (Doniach, 1960). Its incidence in elderly women and association with complement-fixing anti-thyroid antibodies have been shown by Goudie *et al.* (1959).

It would seem reasonable to suggest that the coexistence of the anterior hypophysitis, focal thyroiditis, and atrophic gastritis with pernicious anaemia is not fortuitous. Pernicious anaemia and chronic thyroiditis are now believed to be diseases in which autoimmune processes play an important part. In the present case the pituitary, thyroid, and gastric changes may be explained by the onset of autoimmune reactions to these three glands. It seems likely that the process had been present since at least the time of her first admission to hospital in 1963. Goudie and Pinkerton (1962) suggested that the autoimmune process in their case might have been related to the release of antigens after puerperal involution of the pituitary and thyroid. There is no obvious precipitating factor in the present case. We suggest that anterior hypophysitis of possible autoimmune origin has now to be added to the list of aetiological factors causing hypopituitarism.

Summary

A case is reported of hypopituitarism in a woman aged 74 who suffered from pernicious anaemia. The anterior pituitary and thyroid showed acinar atrophy, fibrosis, and lymphocytic infiltration, and the stomach showed changes of chronic atrophic gastritis. We suggest a possible autoimmune basis for all three lesions.

Thanks are due to Mr. G. R. Headden for the photomicrographs.

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Preliminary Communications

Preliminary Report on Tyramine Headache

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It is well known that a small minority of patients who give a typical history of migraine believe that certain foods precipitate their attacks. The foods most commonly implicated are chocolate, milk and milk products, alcohol, and fish. Reports of investigations into food factors in migraine have produced a variety of conflicting results,[1–7] but no reason for this reaction to certain foods has been established.

In the past three years Blackwell and his associates (Blackwell,[8] Blackwell and Mabbitt,[9] and Blackwell and Marley,[10]) have reported that patients being treated with monoamine oxidase inhibitors occasionally develop severe headaches after eating cheese, and they have shown that these headaches are due to the absorption of tyramine from the cheese owing to the inhibition of monoamine oxidase, the enzyme responsible for the breakdown of tyramine in the intestine. Other foods which caused the same effect were mentioned by Blackwell and Marley.[10]

On reading these reports the similarity between their list of foods and those that can precipitate migraine was apparent.

Table I gives a list of foods mentioned in the literature as migraine precipitants. For comparison a list is also given of foods which are known to have produced severe headache and pressor reactions in patients on monoamine oxidase inhibitors. It may well be that tyramine is not the only amine that could be concerned in the headache due to diet, but this preliminary investigation is concerned with tyramine only.

Since migraine is a hereditary disorder, some migraine sufferers might have a genetic enzyme deficiency (possibly of monoamine oxidase). Such a deficiency might lead occasionally to increased amine levels in the blood stream. A possible explanation of some attacks of migraine may be that certain people have a particularly sensitive localized vascular response to circulating amines such as tyramine.

TABLE I.—*Food Mentioned in Literature as Migraine Precipitants*

Food	Reported to Precipitate Attacks of Migraine	Reported to Precipitate Pressor Reactions and Headache in Patients on M.A.O.I.
Alcohol	+ 2, 13*	+ 8, 9, 10*
Cheese	+ 5, 12	+ 8, 9, 10
Fish	+ 1, 2, 3, 5	+ 8, 9, 10
Beans	+ 1	+ 8, 9, 10
Milk dairy products	+ 1, 2, 5, 13	+ 8, 9, 10
Chocolate	+ 2, 3, 5, 11, 14	+ 15
Eggs	+ 1	
Wheat	+ 1, 5, 13	
Nuts	+ 1, 12	
Tomatoes and other foods	+ 13	

* Reference numbers.

On the basis of these suggestions an experiment was designed to ascertain whether migraine attacks could be precipitated by giving patients tyramine by mouth.

Method

Patients who gave a history of a clear dietary relationship to their attacks of migraine were selected from those attending the migraine clinic at the Elizabeth Garrett Anderson Hospital. The original diagnosis of migraine had been made by a neurologist in all these patients. Though about half the patients questioned gave a history of food factors in relation to their attacks, the information was often unreliable, being influenced by various factors such as articles read in health journals. Where the implicating factors were so diffuse as to invalidate

a dietary history a few patients were included under the heading of "possible dietary" in this investigation. It was decided that only those patients who actually excluded from their diet those foods which they thought precipitated their attacks of migraine could be regarded as reliable. All four of the dietary patients excluded chocolate from their diet. Three also excluded alcohol and the fourth was a teetotaller. In addition one (Case 2) suspected and excluded liver, kidney, and cheese, and another (Case 3) excluded oranges.

Patients with a blood pressure over 140/90 were not included, nor were patients with any history of psychiatric treatment. No patient being treated with any monoamine oxidase inhibitor drug was included.

The patients were asked to take part in an investigation of dietary factors as a cause of migraine. They were told that various capsules would be sent to them by post with instructions on how they should be taken. A questionary to be completed and returned 24 hours after taking the capsule was also sent. They were told that the capsules would look identical but would contain extracts of food substances which might or might not precipitate an attack of migraine.

Capsules containing 100 mg. of tyramine were used. This is roughly the amount of tyramine that could be found in 3½ oz. (100 g.) of a cheese rich in tyramine. Identical-looking capsules containing 100 mg. of lactose were used as a control.

The results on the patients studied are shown in Table II, and the clinical features of their attacks in Table III.

TABLE II.—*Response to Tyramine and Lactose*

Patient Group	Lactose 100 mg.	Tyramine 100 mg.	Repeat Tyramine 100 mg.
Dietary history			
1	0	+	+
2	0	+	+
3	0	+	+
4	0	+	+
Non-dietary history			
5	0	0	
6	0	0	
7	0	0	
8	0	0	0
Possible dietary history			
9	0	0	
10		+	0
11	Headache all day before lactose and after. Repeat lactose 0	+	
12	0	0	0

+ = Headache.

TABLE III.—*Clinical Features of Response to Tyramine in Patients with Dietary History*

Patient Case No.	Time Tyramine Taken	Time of Onset of Attack	Duration of Attack (Hours)	Headache	Nausea	Vomiting	Eye Symptoms	Typical of Patient's Usual Attack
1	5.00 p.m.	6.30 p.m.	12½	Unilateral	+	0	+	+
	5.15 „	6.00 a.m.*	24	„	+ +	+ +	+ +	+ +
2	4.30 „	6.30 p.m.	22	„	+ +	+ +	+ +	+ +
	5.15 „	4.00 a.m.	18	„	+ +	0	+ +	+ +
3	4.00 „	6.00 p.m.	7	„	+	0	+	+
	4.30 „	8.00 a.m.*	8	„	+	0	+	+
4	4.00 „	2.30 a.m.*	11½	Generalized	+	0	+	+
	4.15 „	2.30 a.m.*	3	„	+	0	+	+

* All these patients said they were awakened by their headache.

DISCUSSION

The precipitation of an attack of migraine by a dose of 100 mg. of tyramine in those patients who gave a clear dietary history, and the failure to precipitate an attack in the same patients by giving lactose, suggests that it is possible that tyramine may be one of the causal agents of the attacks of migraine in these patients. The fact that no attacks were reported while the patients were on lactose suggests that a psychological explanation of migraine is not likely, at any rate in this group.

The interest of these preliminary results is so considerable that further work has been planned to confirm and elucidate the findings.

Studies on the presence of monoamine oxidase in intestinal biopsies are being arranged. If lack of monoamine oxidase is the basic defect it might be possible to administer the enzyme with food and so protect this group of patients with dietary migraine from attacks. A list of foods containing tyramine is also being compiled.

Further studies on the metabolism of tyramine and its effect on the cerebral circulation are being arranged.

It is also necessary to consider whether patients with a history of migraine who do not get an attack when given tyramine may in fact absorb it under certain conditions; for instance, if their monoamine oxidase is inhibited—for example, monoamine oxidase levels are known to vary in women at different phases of the menstrual cycle.

It is possible that the ingestion of a small amount of tyramine will provide a helpful test in elucidating the cause of repeated headache in patients in whom known causes have first been excluded.

Another point of interest is that alcohol is constantly mentioned by patients as a dietary precipitant of migrainous attacks. Possibly alcohol facilitates the absorption of tyramine, and circulating tyramine may be a factor in the headache associated with the drinking of alcohol.

It may well be that tyramine is not the only amine in food that can produce this effect in susceptible individuals, and further clinical work is necessary. I would be most grateful if anybody who knows of patients with a clear-cut dietary history of migraine would kindly contact me, as further patients are needed for this study.

SUMMARY

A preliminary experiment is described in which patients with a history of migraine precipitated by food were given 100 mg. of tyramine or 100 mg. of lactose in a controlled trial. Migraine was precipitated by the tyramine but not by the lactose. The implications of these findings and the future work in progress are discussed.

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