# Thyrotoxic vomiting

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## Summary

**In seven patients vomiting played an important part in the presentation of thyrotoxicosis. Vomiting does not always indicate severe thyroid disease, and the diagnosis in patients presenting with this symptom may be long delayed.**


## Introduction

An increased appetite with weight loss is accepted as being one of the cardinal symptoms of thyrotoxicosis. Only infrequently do patients complain of anorexia. Under modern conditions nausea and vomiting appear to be rare complications of thyrotoxicosis. We describe here seven cases of vomiting in thyrotoxicosis. Two of our patients presented with prolonged intermittent vomiting, and thyrotoxicosis was not suspected until late in the disease.

## Case 1

In January 1971 a 41-year-old woman presented with anorexia, nausea, vomiting, and faintness. She also had had continuous aching in the epigastrium and had taken an aspirin-containing compound. In the next three weeks she vomited blood on three occasions and passed melaena stools on the three days before her admission on 19 February.

On examination her blood pressure was 140/90 mm Hg and her pulse rate 120/min, but there was no other abnormality. The abnormal findings on investigation were an initially raised blood urea concentration of 9 mmol/l (54 mg/100 ml), though this later fell to normal. The plasma cholesterol concentration was 2·15 mmol/l (83 mg/100 ml), bilirubin was raised at 25 μmol/l (1·5 mg/100 ml), and the serum aspartate and alanine transferase levels were raised at 120 IU/l and 72 IU/l respectively. Her alimentary bleeding was thought to be the result of aspirin ingestion, but the abnormal liver function test results were not explained. She became free from symptoms and was discharged on 9 March 1971.

During the next six months she was readmitted twice with abdominal pain, dizziness, vomiting, diarrhoea, and depression. The investigations were repeated, but the results were basically unchanged. A raised protein-bound iodine concentration of more than 1600 nmol/l (20·3 μg/100 ml) was attributed to contamination. On 17 September, when in the outpatient department, she appeared anxious, warm, sweaty, and tremulous. She still suffered from abdominal pain and occasional vomiting, and had lost 20 kg. She was thought clinically to be thyrotoxic, and on radioactive $^{131}I$ uptake test the four-hour uptake was 83% of the ingested dose (normal $\leqslant 40\%$), and the 48-hour protein-bound $^{131}I$ was 2·88% (normal $\leqslant 0{\cdot}4\%$), confirming the diagnosis. Fluorescent autoantibodies to thyroid cytoplasm were present.

She was started on carbimazole, and over the next four months her symptoms disappeared and she became euthyroid. The liver function test results returned to normal.

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## Case 2

A 35-year-old woman had suffered from ulcerative colitis affecting the descending and sigmoid colon since 1969. Her bowel symptoms were well controlled on oral sulphasalazine. In March 1971 she started to have attacks of vomiting without apparent cause. The vomiting lasted for one or two days, and she began to lose weight and became pigmented. In August 1971 the vomiting became more severe. When admitted on 7 November 1971, she had lost 16 kg and had vomited continuously for four days. She was dehydrated and pigmented; the buccal mucosa was pigmented also. The blood pressure was 110/80 mm Hg. Routine investigations gave normal results. She was thought to be in Addisonian crisis and was treated with intravenous saline and hydrocortisone. She improved rapidly and was discharged on 15 November, taking fludrocortisone 0·1 mg daily and cortisone 25 mg twice daily. Autoantibodies had not been found.

During the next 11 months she was admitted three times with bouts of vomiting. During the admission in May 1972 the plasma cortisol concentration was 140 nmol/l (5·1 μg/100 ml), but there was insufficient evidence that the vomiting was due to Addison's disease. After her admission on 24 October 1972 she developed auricular fibrillation, and the protein-bound iodine was over 1600 nmol/l (20·3 μg/100 ml). The diagnosis of thyrotoxicosis was confirmed when radioactive $^{131}I$ uptake was 73% of the ingested dose at four hours, and 48-hour radioactive protein-bound iodine was 1·99% of the ingested dose. Thyroid autoantibodies were not present. She was started on carbimazole and improved greatly; her vomiting ceased, and her pulse reverted to sinus rhythm. She was stabilised on carbimazole 5 mg twice daily, cortisone 12·5 mg thrice daily, and fludrocortisone 0·1 mg daily.

## Case 3

A 49-year-old woman developed palpitations, occasionally associated with a dull pain in the chest, in December 1972. In June 1973 she started opening her bowels 10 times a day. She became severely anorexic and vomited after most meals. In August 1973 she became short of breath on effort and her ankles were swollen. She was treated with propranolol 40 mg thrice daily.

In September 1973 she looked ill and was breathless at rest, with a definite fine finger tremor. She had atrial fibrillation at a rate of 108/min. The thyroid was diffusely enlarged and a soft bruit audible. A lid lag was evident and there was considerable sacral and leg oedema. Her serum protein-bound iodine concentration was over 1600 nmol/l (20·3 μg/100 ml), and Thyopac 3, Thyopac 4, and free Thyopac index confirmed her to be thyrotoxic. Antibodies to thyroid cytoplasm were present in high titres. An electrocardiogram (ECG) confirmed atrial fibrillation, and a chest *x*-ray film showed cardiomegaly, but all other investigations were normal.

She was treated with carbimazole, digoxin, diazepam, and a diuretic. She improved rapidly, became euthyroid, and her anorexia and vomiting improved rapidly. The atrial fibrillation persisted for a period.

## Case 4

A 66-year-old woman presented in September 1973 with a three-month history of vomiting after most meals, weight loss, slight difficulty in swallowing, and a burning retrosternal pain. Seven years earlier she had been shown to be thyrotoxic but had not vomitted. She was clinically thyrotoxic and had swelling of the right lobe of the thyroid. Physical examination was otherwise normal. The protein-bound iodine concentration was 1600 nmol/l (20 μg/100 ml) and a four-hour $^{131}I$ uptake 75%. Thyroid gammascan was normal. A chest radiograph showed that the heart size was at the upper limit of normal and that there was minimal compression of the trachea.

The patient was placed on carbimazole 30 mg daily and practolol 100 mg thrice daily. She soon became euthyroid, her weight increased, and the vomiting stopped.

## Case 5

In mid-November 1973 a 57-year-old woman developed exertional dyspnoea, central chest discomfort, and, within two weeks, swelling below the knees at night. Early in December 1973 she developed aversion to tea, coffee, and cigarettes and started to have nausea with vomiting. About a week later she had diarrhoea for one day and complained of faintness on standing. Her blood pressure was 110/50 mm Hg and pulse rate 115/min, and she had oedema below the knees. The liver was slightly tender and enlarged one finger's breadth below the costal margin. The thyroid was palpable.

On 4 January 1974 her vomiting had become much more severe, and she could not keep down even water. She had lost 4 kg in a week. The blood pressure was 110/70 mm Hg and the pulse rate 140/min. The thyroid was firm but not enlarged, and the liver was still enlarged. There was no exophthalmos, sweating, or tremor. She was admitted to Edinburgh Royal Infirmary and required intravenous fluids for the next ten days. Extensive radiological and laboratory investigations yielded normal results. Thyrotoxicosis was diagnosed when an $^{131}I$ uptake was 60% of the administered dose at four hours and the effective thyroxine ratio 1·50 (normal 0·83-1·10). Thyroid autoantibodies were not present. A thyroid scan was normal, and the serum cholesterol level was 4 mmol/l (154 mg/100 ml).

Treatment was with digoxin, practolol, and chlorpromazine. Radioactive iodine therapy was given in January 1974, followed by carbimazole. When discharged on 30 January she was much improved and no longer vomiting, and she had a pulse rate of 80/min.

## Case 6

A 66-year-old woman presented in October 1974 with a seven-week history of shortness of breath on effort and ankle swelling. For two weeks she had experienced severe anorexia, nausea, and repeated vomiting. Her weight was steady, but she complained of generalised weakness and slight sweating. Thirteen months earlier, during radiotherapy for carcinoma of the breast, she had complained transiently of nausea. Recent drug treatment had consisted of digoxin and a diuretic.

She was pale, with a small nodule palpable at the base of the neck to the right of the trachea, in the suprasternal notch. It was not known whether this was a thyroid nodule or possibly a metastasis. There was no other lymphadenopathy. There was a mild tremor and lid lag and a sinus tachycardia of 130/min. Physical examination was otherwise normal. She was thought to be thyrotoxic, the nausea being attributed to digoxin toxicity. Nevertheless, neausea and vomiting persisted after she stopped taking digoxin.

Investigations showed a protein-bound iodine over 1600 nmol/l (20·3 μg/100 ml), and Thyopac 3 and 4 and the free Thyopac index confirmed her to be thyrotoxic. Additionally, the $^{131}I$ uptake was 76% at 24 hours and 64% at 48 hours. Thyroid scan was normal, and thyroid antibodies were present only to thyroglobulin in moderate titre. Serum sodium concentration on admission was low at 129 mmol/l (129 mEq/l), as was the serum potassium at 2·9 mmol/l (2·9 mEq/l). Blood urea and bicarbonate were slightly raised at 13 mmol/l (78·3 mg/100 ml) and 29·8 mmol/l (29·8 mEq/l) respectively. These findings were thought to be consistent with repeated vomiting. An ECG showed no obvious signs of digoxin toxicity. No evidence of secondary deposits was found.

The patient was therefore thought to be thyrotoxic and the vomiting a manifestation of her hyperthyroidism. Radioactive iodine was given in suitable dosage and followed by carbimazole. She improved rapidly and had no further episodes of vomiting.

## Case 7

A 54-year-old man presented in January 1976 with a four-week history of poor appetite and nausea after meals, which was relieved by vomiting. He had lost 2·5 kg and had also noticed palpitations and breathlessness on effort. He was thin with slightly prominent eyes and a sinus tachycardia of 120/min and blood pressure of 120/70 mm Hg. The liver was enlarged one finger's breadth below the costal margin. Swelling and limited movement of the proximal interphalangeal joints of both hands was attributed to a minor degree of rheumatoid arthritis.

An ECG showed sinus tachycardia, with normal QRS complexes and runs of auricular fibrillation. The abnormal findings on investigation were a raised alanine aminotransferase (160 U/l), a raised protein-bound iodine (1219 nmol/l (15·5 μg/100 ml)), and T3 and T4 values which confirmed thyrotoxicosis. Radioimmune assay showed that the tri-iodothyronine concentration was considerably raised (over 25 nmol/l (16·3 ng/ml)), but autoantibodies were not found, and the serum cholesterol was low at 2·5 nmol/l (97 mg/100 ml).

He was started on carbimazole 30 mg daily and propranolol 40 mg four times daily. His vomiting stopped completely within 24 hours; he became euthyroid; and the liver function tests returned to normal.

## Discussion

Vomiting as a symptom of thyrotoxicosis appears to have been partially forgotten. The standard text, *Fundamentals of Clinical Endocrinology*,[1] does not mention vomiting as a feature of the presentation of Graves's disease in adults, and Beeson and McDermott's *Textbook of Medicine*[2] does not either—though the latter do regard it as a feature of a thyroid crisis, which they define as a sudden severe exacerbation of hyperthyroidism. Nevertheless, some modern books do mention vomiting and nausea as occasional features of hyperthyroidism.[3 4]

Thyrotoxic vomiting, however, was certainly known to earlier physicians, and Osler's *Principles and Practice of Medicine*[5] vividly describes such a case. Cameron[6] in 1945 knew it also, although he felt it a symptom of crisis or near crisis, as have others.[7 8]

Advances in treatment and earlier diagnosis seem to have made severe thyrotoxicosis less common and the duration of toxicity shorter. Five patients (cases 3, 4, 5, 6, and 7) were thought to have moderately severe disease of the thyroid, as shown by shortness of breath, ankle swelling, palpitations, or recent weight loss—though they were certainly not in crisis. Cases 1 and 2 are of particular interest; in these patients vomiting was intermittent, prolonged, and apparently unaccompanied by other symptoms of thyrotoxicosis. Clinically this led to considerable difficulty and resulted in considerable delay in diagnosis.

There was no evidence of any hypermetabolism of the central nervous system that might have directly stimulated the vomiting centre in the medulla.[9] Only three patients (cases 1, 2, and 3) had diarrhoea; in one (case 1) it was less frequent than the vomiting, and another (case 2) had ulcerative colitis. It seems unlikely that vomiting was due to increased activity of the gastrointestinal tract. Vomiting in other endocrine conditions, such as hyperparathyroidism, Addisonian crisis, diabetic ketosis, and pregnancy is almost certainly induced by stimulation of the chemical trigger zone, and this is the likely mechanism in thyrotoxicosis. The vomiting was abolished by carbimazole in all our patients, indicating that thyroid hormone had initiated the vomiting.

There was no evidence of any serious metabolic disorder other than thyrotoxicosis in our patients. One patient (case 2) appeared to have Addison's disease, but for clinical reasons it was possible to obtain only an isolated cortisol level of 140 nmol/l, which was inappropriately low. Even here the vomiting persisted after adequate treatment of the hypoadrenalism with intravenous saline and hydrocortisone, and later with oral cortisone and fludrocortisone. Although concentrations of liver enzymes were slightly raised in cases 1, 5, 6, and 7, the liver function test results were not thought to be sufficiently deranged to be responsible for the vomiting, and the enzymes returned to normal values with treatment. Abnormal liver function tests, which may occur in thyrotoxicosis, are evidence of mild structural and functional disturbances of the liver, the commonest finding being of depletion of liver glycogen and increased fatty infiltration.[10]

In reporting these cases we aim at drawing attention to this forgotten symptom of thyrotoxicosis, and particularly to emphasise that at times vomiting may be the only presenting feature, leading to considerable difficulty in diagnosis.

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# Mode of presentation of juvenile diabetes

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## Summary

**In a study of 66 children with juvenile diabetes symptoms had often been present for over a month before diagnosis. Though polyuria, polydipsia, and weight loss were the commonest features, other important symptoms included tiredness, lethargy, and malaise. A gradual onset of diabetes was commoner than is generally realised.**

## Introduction

Although juvenile diabetes is uncommon it is important for all doctors treating children to be alert to the different ways in which it may present. We performed a study, reported here, to determine the mode of onset of diabetes in children and to estimate delays in diagnosis.

## Patients and methods

Sixty-six children (35 boys and 31 girls) below the age of 17 years (the youngest being 21 months of age) who presented with juvenile diabetes in two district hospitals over nearly three years (January 1972 to November 1975) were studied. Nine other children presenting with diabetes over this period were excluded because details of their admission were inadequate or we had difficulty in tracing them for follow-up.

Most of the information about symptoms and delay in diagnosis was obtained from an interview with the parents and, in the case of the older children, with the children themselves. All the hospital notes, including the general practitioner's initial referral letter, were also carefully examined.

## Results

### SYMPTOMS

The classical symptoms of juvenile diabetes—namely, polyuria, polydipsia, lethargy, and weight loss—were, not surprisingly, the four commonest presenting symptoms in this series (see table). Sixty-four children had polydipsia; 61 had polyuria; 59 had lethargy, malaise, and tiredness; and 48 had weight loss. One interesting finding was a high incidence of secondary enuresis (25 children). Irritability was noted in 17 children. Seven children had blurring of vision before diabetes was diagnosed, while six presented in severe diabetic ketoacidosis. Two children were found to be diabetic on routine urine analysis when attending hospital for other conditions.

*Duration of symptoms before diabetes was diagnosed in 66 children*

| Duration (weeks): | <1 | 1- | 2- | 4- | ⩾8 | Unknown | Total No of children with each symptom |
|---|---|---|---|---|---|---|---|
| Polydipsia .. | 20 | 16 | 9 | 13 | 5 | 1 | 64 |
| Polyuria .. .. | 21 | 13 | 9 | 12 | 5 | 1 | 61 |
| Lethargy .. .. | 14 | 12 | 9 | 11 | 9 | 4 | 59 |
| Weight loss .. | 11 | 6 | 5 | 12 | 5 | 9 | 48 |
| Abdominal pain .. | 15 | 4 | 1 | 7 | 1 | 2 | 30 |
| Enuresis .. .. | 7 | 1 | 4 | 4 | 5 | 4 | 25 |
| Nausea and vomiting | 14 | 2 | 1 | 2 | 1 | 2 | 22 |
| Irritability .. | 4 | 4 | 2 | 3 | | 4 | 17 |
| Visual symptoms .. | 2 | 1 | 1 | | | 3 | 7 |
| Coma .. .. | 6 | | | | | | 6 |

### DURATION OF SYMPTOMS

The estimated duration of the individual symptoms is shown in the table. The exact duration of some symptoms could not be given by some parents. Six of the children had symptoms for under a week, 13 had symptoms for more than one but less than two weeks, and 18 had symptoms for over two weeks but less than a month. The remaining 29 had symptoms for one month or more: one child had polyuria and polydipsia for over a year before diabetes was diagnosed. No correlation was found between the duration of symptoms and the severity of the diabetes on presentation.

The classical symptoms of juvenile diabetes were often present for many days, and, in many of the children, for more than a month. Those symptoms associated with ketoacidosis—notably, nausea, vomiting, and abdominal pain—occurred predominantly in the few days before the diagnosis, but several children complained of abdominal pain some weeks before the diagnosis was made.

Twenty children had an upper respiratory tract infection within a month of diagnosis of diabetes. Mumps, however, was only reported in one child three weeks before diabetes was diagnosed; there was no history of abdominal pain at that time to suggest the presence of mumps pancreatitis.

### MODE OF DIAGNOSIS

In 22 of the children the diagnosis of diabetes was either suspected or made by the parents or, in one case, a brother. There was a history of diabetes in a first-degree relative in nine of the 65 children (excluding one adopted child). This incidence of 14% is comparable

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