thyroid.¹ It is rare for benign goitre to cause paralysis of the cord.² In the only previous case report of a thyroid cyst causing unilateral recurrent nerve palsy the patient had a seven year history of hoarseness and goitre.³ Rapidly progressive bilateral recurrent laryngeal nerve palsy secondary to acute enlargement of a cyst has not been reported.

It is difficult to explain the rapid onset of bilateral nerve compression and the sudden relief of symptoms by operation. Rapid expansion of a cyst, with a sudden general increase in pressure within the confines of the pretracheal fascia sufficient to impair the microcirculation to both recurrent nerves, seems the most likely mechanism—in other words, a pretracheal compartment syndrome. The fact that this does not occur more often may relate to the great variability of this fascial layer and its relations with the recurrent laryngeal nerves. The nerves may be within the fascial compartment proper, invested by the fascial sheath itself, or completely outside the compartment for the whole of their course.⁴

Percutaneous needle aspiration of such a cyst is likely to relieve the pressure on the recurrent nerves sufficiently to reduce dyspnoea and stridor before definitive surgery. This is proposed as the initial treatment when acute enlargement of the cyst or haemorrhage within it compromises the upper airway.

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Remission of symptoms in carcinoid syndrome with a new 5-hydroxytryptamine M receptor antagonist

The principal features of the carcinoid syndrome are flushing and diarrhoea. The tumours often grow slowly, and disabling symptoms may continue for many years. Symptomatic treatment by pharmacological methods or debulking procedures can improve the quality of life of many patients,¹ but the available drugs are often not completely effective. We report on the efficacy of a new drug, [1H]-indol-3-carbonic-acid-tripine-ester-hydrochloride (ICS 205-930, Sandoz, Basle, Switzerland),² one of the first generation of specific 5-hydroxytryptamine M (neuronal) receptor antagonists.³

Patients, methods, and results

We studied three patients (cases 1-3) with secretory diarrhoea due to the carcinoid syndrome and two controls (cases 4 and 5) with similar secretory diarrhoea due to metastatic vasoactive intestinal peptide (VIP) secreting tumours. The first patient was a 72 year old man with a four year history of severe diarrhoea up to 19 times a day. He suffered only occasional flushes but profuse postprandial

sweating. Medication was prednisolone 20 mg/day, azothiaprime 150 mg/day (bullous pemphigoid had been diagnosed two years earlier), and cyproheptadine 12 mg/day. Case 2 was a 41 year old woman with an eight year history of carcinoid disease. She had watery diarrhoea up to 15 times a day and frequent flushing. Medication was cyproheptadine 12 mg/day. Case 3 was a 54 year old man with a two year history of watery diarrhoea and infrequent flushing. Medication was methysergide 1 mg/day. The controls (aged 46 and 50) both suffered secretory diarrhoea due to metastatic VIP secreting tumours. Both were receiving codeine phosphate and loperamide and case 5 was also treated with the somatostatin analogue SMS 201-995.

No changes were made to the subjects' long term medication. Stool collections were weighed daily for three days before the study and repeated while the subjects received a three day course of ICS 205-930 administered by slow intravenous injection. Serial 24 hour urinary 5-hydroxyindole acetic acid estimations were made throughout the period.

The diarrhoea improved considerably in the three patients with carcinoid syndrome but not in the controls (table). Flushing in the patients with carcinoid syndrome did not change, but sweating improved considerably in the one patient in whom it was troublesome (case 1). Urinary 5-hydroxyindole acetic acid excretion was unchanged in all subjects (table).

One of the five subjects (case 2) developed fever (peak temperature 39°C) 36 hours after starting treatment, and the drug was stopped. She had suffered continuous diarrhoea for four years, and this symptom had resolved completely during this first day of treatment. Two months later rechallenge at a lower dose (20 mg daily) on two days was again followed by a fever, strongly suggesting an idiosyncratic drug reaction. The four other subjects tolerated the drug well.

Comment

Peripheral 5-hydroxytryptamine receptors have been divided into two groups.⁴ The D receptors exist mainly on smooth muscle cells, and the M receptors are primary neuronal, acting by modulating the release of other neurotransmitters. Several antagonists of the D (smooth muscle) receptors (such as methysergide) have been developed, which either have proved poorly effective in the carcinoid syndrome or have unacceptable toxicity.⁵ The specific symptomatic response produced by ICS 205-930 in our three patients suggests that 5-hydroxytryptamine M receptors mediate the secretory diarrhoea of the carcinoid syndrome and may be partially implicated in the sweating. Diarrhoea in the carcinoid syndrome may also, of course, be due to bacterial overgrowth or bile salt spillage or develop as a postoperative complication, and specific therapies would be necessary in these circumstances.

This study suggests that 5-hydroxytryptamine M receptor antagonist drugs will have an important role in the symptomatic treatment of watery diarrhoea in the carcinoid syndrome. The assessment of this new class of drug in other conditions in which 5-hydroxytryptamine overreactivity may be implicated is awaited with interest.

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Details of symptoms and treatment in three patients with carcinoid syndrome and two with vipomas

Case No	Mean stool weight (g/day)		Mean stool frequency (motions/day)		Mean urinary 5-hydroxyindole acetic acid (μmol/24 h)		Daily dose of ICS 201-950 (mg on each day)
	Before	During	Before	During	Before	During	
1	1163	702	12	6.3	1100	1107	30/30/30
2	421	173	7.0	2.0	793	511	30/20/nil
3	471	294	6.7	1.7	1333	1421	20/20/20
4	2767	2107	9.3	10.3	6	34	20/20/20
5	516	584	3.7	4.7	23	16	10/20/20