he painted white spirit on to cardboard for 15 minutes without appreciable change in his $FEV_1$ or histamine $PC_{20}$. On the first test day he brush painted the accelerator (1% cobalt octoate in styrene) for two minutes he developed a dual asthmatic response with a decrease in histamine $PC_{20}$ from 2·3 mg/ml before the test to 0·5 mg/ml 24 hours after the test. Two days later brush painting of styrene alone for one minute provoked a similar dual asthmatic response with a similar reduction in histamine $PC_{20}$—from 2·7 to 1·3 mg/ml 24 hours after the test. Brush painting with 20 ml pure styrene on another day, which generated an atmospheric styrene concentration of 12 ppm (Gastec colorimeter method, threshold limit value 100 ppm) provoked a similar dual asthmatic response. Mandelic acid, the principle metabolite of styrene,[1] was not detected in the patient's blood or urine, which were sampled immediately and 24 hours after this exposure.

The patient was told of the cause of his asthma and has subsequently avoided exposure to styrene at work. Six months after diagnosis he remains well and uses his bronchodilator inhaler only before strenuous exercise.

## Discussion

Styrene or phenylethylene ($C_6H_5CHCH_2$) was used by this patient for the production and repair of fibreglass moulds. The only previous report of asthma associated with occupational exposure to styrene[2] described two patients in whom inhalation tests with styrene provoked an immediate asthmatic response. The authors therefore were not able to distinguish whether an irritant or a hypersensitivity response was the cause of the asthma. The findings in this case are consistent with asthma as a manifestation of a specific hypersensitivity response to styrene. Exposure to styrene in an atmospheric concentration of 12 ppm (TLV 100 ppm), insufficient for mandelic acid to be detectable in blood or urine, reproducibly provoked both an immediate and a late asthmatic response and an associated reduction in histamine $PC_{20}$. Styrene seems able to initiate asthma by inducing a specific hypersensitivity response.

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*Thorax* 1991;**46**:397–398

# Long survival after excision of a primary malignant melanoma of the oesophagus

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## Abstract

**A woman who had a large primary malignant melanoma of the oesophagus, with evidence of submucosal invasion and several local metastases, underwent resection two years after the onset of retrosternal pain and has survived for 12 years with no recurrence.**

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Accepted 15 February 1991

Primary malignant melanoma of the oesophagus is an extremely rare tumour associated with poor survival. Of the 115 cases reported worldwide, the five year survival is 4%.[1] The treatment of choice is surgical resection. We present a patient with primary malignant melanoma of the oesophagus who survived 12 years after surgery.

## Case report

A 40 year old woman presented with a two year history of retrosternal pain associated with progressive dysphagia and weight loss (6 kg in four months). She had no important past medical history and physical examination showed nothing remarkable. Haematological and biochemical investigations gave results within normal limits. Barium swallow examination showed a large, irregular soft

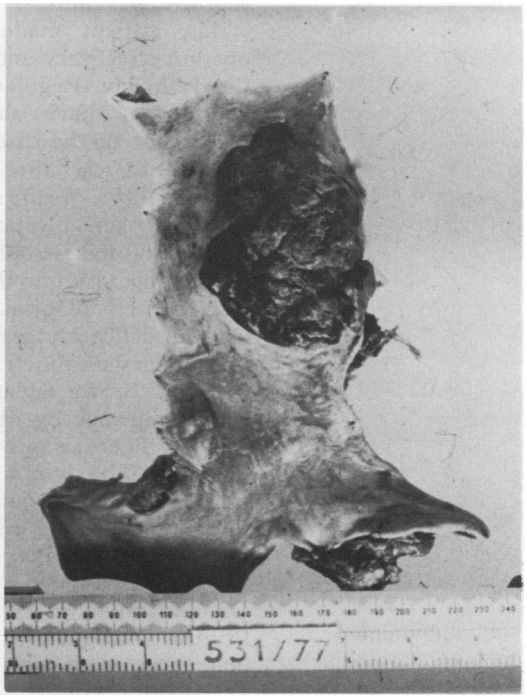


*Figure 1 Resected specimen showing an ulcerated black fungating tumour of the lower oesophagus. At its widest the specimen is 17 cm.*

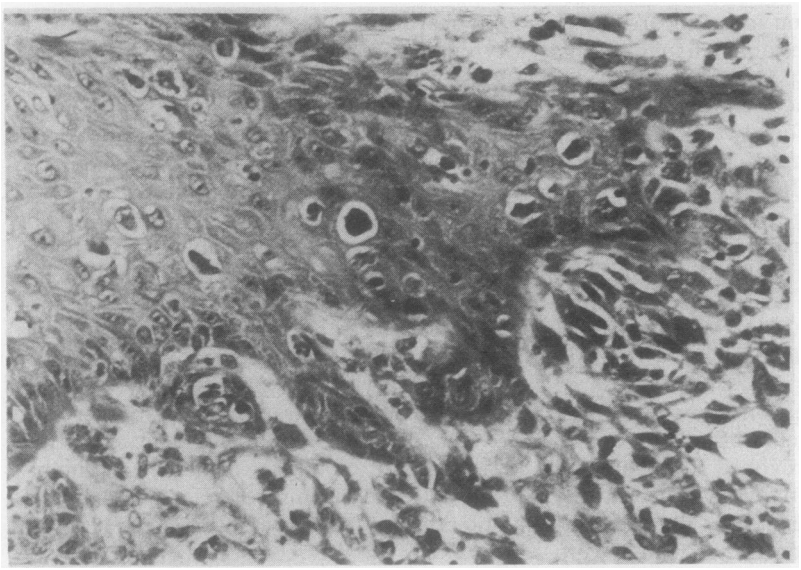

*Figure 2 Photomicrograph of the ulcerated edge of the tumour seen in figure 1, showing primary malignant melanoma of the oesophagus arising from atypical junctional activity. (Haematoxylin and eosin.)*

tissue mass in the middle and lower oesophagus. Endoscopy showed a large, necrotic, polypoid, black tumour at 25 cm, almost completely obstructing the lumen. Biopsy samples were taken and histological examination showed appearances consistent with primary malignant melanoma.

At surgery a large oesophageal tumour was found to extend from the level of the azygos vein to below the hilum of the right lung. The stomach and mediastinum were free of tumour but there were numerous black lymph nodes in the lesser omentum. The stomach was mobilised along its greater curvature to form a conduit; a vagotomy and pyloroplasty were performed. A subtotal oesophagogastrectomy was carried out with an intrathoracic anastomosis.

The patient made an uneventful postoperative recovery and was allowed home on the 12th day. Regular follow up and repeat endoscopies have shown no evidence of recurrence of the disease. She remains alive and well 12 years after surgery.

*Pathological findings* In the resected specimen an ulcerated, black, fungating tumour of the oesophagus, 9 × 6 cm and protruding 3 cm into the lumen, was identified (fig 1). Histological examination showed characteristic changes of primary malignant melanoma with junctional activity, ulceration, and dark brown melanin pigment in tumour cells, confirmed by Masson Fontana staining (fig 2). There was evidence of submucosal invasion. The lymph nodes near the main bulk of the tumour, at the gastro-oesophageal junction and in the lesser omentum, contained metastatic melanoma.

## Discussion

Primary malignant melanoma of the oesophagus is rare. In a series of 1910 patients with malignant tumours of the oesophagus, Turnbull *et al* reported two cases of primary malignant melanoma (0·1%).[2] We have found 115 cases reported worldwide, the first by Bauer in 1906.[3] The mean presenting age was 59 (range 7–81) years and the male:female ratio 2:1. The patients presented with symptoms similar to those caused by other malignant tumours—namely, dysphagia, retrosternal pain, vomiting, weight loss, regurgitation, epigastric or chest pain, coughing, and sialism.

The occurrence of primary malignant melanoma, a malignant tumour of melanocytes, in the oesophagus is not unexpected in view of the reported presence of melanocytes in the epidermal basal layer in about 4% of the normal population.[4] Melanocytes, which are melanin pigment producing cells derived from the neural crest, are believed to migrate to the oesophagus during embryogenesis in the same way they migrate to the skin and other sites.[5] In 1952 Allen and Spitz[6] set criteria for the diagnosis of primary malignant melanoma of mucous membranes, and these were subsequently reiterated for the oesophagus by Raven and Dawson.[7] The case reported here adequately fulfils these criteria in that atypical melanocytes proliferated in the epidermal basal layer (atypical junctional activity) and there was stromal invasion by neoplastic melanocytes containing demonstrable melanin pigment.

Diagnosis of primary oesophageal malignant melanoma requires a combination of investigations, including barium contrast studies, which may show a polypoid, irregular defect in the oesophageal lumen; oesophagoscopy, showing an ulcerated polypoid black or pink tumour; and finally biopsy with histopathological assessment.

The treatment of choice is surgical resection with re-establishment of gastro-intestinal continuity. However, the prognosis remains poor, with an overall survival of 4·2% at five years. The case described here appears to be the first reported of such long survival after surgery and leads us to believe that surgical resection should be attempted whenever possible, even in the presence of lymph node metastases.

We are grateful to Mr A G Norman for allowing us to report his case.

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