

# Correspondence

## Pulmonary vascular lesions in the toxic oil syndrome in Spain

SIR,—I read with great interest the article on the toxic oil syndrome in Spain by WP Fernández-Segoviano and others (October 1983;38:724). Although the basic toxic agent found in the denatured rapeseed oil ingested by their patients might be oleonilid as they described, the possibility of poisoning by polychlorinated biphenyls (PCBs) should be taken into consideration. PCBs have been widely used as a heat transfer agent and as an insulator in electrical equipment. Paints and other surface coatings such as plastics and varnishes may also contain PCBs. The denatured rapeseed oil imported from France was originally for industrial use and was treated by a "refining" process for food use in Spain. It is probable that denatured rapeseed oil had contained PCBs or that dedenatured oil had been contaminated with PCBs.

In fact, the world's largest and first major episode of food poisoning by PCBs occurred in Japan in 1968.<sup>1</sup> The disease called "yusho" (Japanese for "oil disease") is acute or subacute poisoning due to ingestion of "Kanemi rice oil" contaminated with PCBs. PCBs, used as a heat transfer medium in a deodorising process, had leaked from stainless steel pipes into the cooking oil mixture during Kanemi's manufacturing of cooking oil from rice bran. About 13 000 persons who had ingested contaminated cooking oil were affected.<sup>1</sup> By 1979 the Government had officially designated 1665 sufferers of the disease, including 53 deaths. The disease is characterised by various dermal, respiratory, gastrointestinal, endocrinological, and neurological manifestations.

There seems to be some relationship between toxic oil syndrome in Spain and yusho in Japan. Has the possibility of PCB poisoning ever been ruled out by measuring the concentration of PCBs in the blood and tissues of patients with toxic oil syndrome?

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<sup>1</sup> Reich MR. Kanemi oil poisoning incident. In: *Kodansha encyclopedia of Japan* (4). Tokyo: Kodansha, 1983.

## Diagnosis of lung cancer by fiberoptic bronchoscopy: problems in the histological classification of non-small cell carcinomas

SIR,—In their paper on diagnosis of non-small cell lung carcinoma by fiberoptic bronchoscopy (March 1984; 39:175) Dr MT Chuang and colleagues reported that in 38% of 107 cases the histological type found in a resected specimen differed from that previously diagnosed from bronchoscopic biopsy specimens. The authors did not refer

to two similar studies which found disagreement between bronchoscopic biopsy specimens and eventual diagnosis in only 9.1% of 233 cases<sup>1</sup> and 11.7% of 94 cases<sup>2</sup> of non-small cell lung carcinoma. Diagnostic criteria were similar in all three studies.

Dr Chuang and his colleagues suggested that the inaccuracy of prediction of cell type might be due to the small size of biopsy specimens taken through the fiberoptic bronchoscope. However, it has been shown that the error rate for cell type prediction is no greater with fiberoptic bronchoscopic biopsy specimens than with the larger biopsy specimens obtained at rigid bronchoscopy.<sup>2</sup> It has been shown that the diagnostic yield of fiberoptic bronchoscopic biopsies increases with the number of specimens taken<sup>3</sup> and the experience of the bronchoscopist.<sup>4</sup>

Factors responsible for the variable diagnostic accuracy of bronchoscopic biopsy reported in various studies may include the number of samples taken at each bronchoscopy and the skill of the bronchoscopists and pathologists concerned.

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<sup>1</sup> Payne CR, Hadfield JW, Stovin PG, Barker V, Heard BE, Stark JE. Diagnostic accuracy of cytology and biopsy in primary bronchial carcinoma. *J Clin Pathol* 1981;34:773-8.

<sup>2</sup> Rudd RM, Gellert AR, Boldy DAR, *et al*. Bronchoscopic and percutaneous aspiration biopsy in the diagnosis of bronchial carcinoma cell type. *Thorax* 1982;37:462-5.

<sup>3</sup> Gellert AR, Rudd RM, Sinha G, Geddes DM. Fiberoptic bronchoscopy: effect of multiple bronchial biopsies on diagnostic yield in bronchial carcinoma. *Thorax* 1982;37:684-7.

<sup>4</sup> Gellert AR, Rudd RM, Sinha G, Geddes DM. Fiberoptic bronchoscopy: effect of experience of operator on diagnostic yield of bronchial biopsy in bronchial carcinoma. *Br J Dis Chest* 1982;76:397-9.

\*\*This letter was sent to the authors, who reply below.

SIR,—Drs Gellert and Rudd are correct to bring articles with supposed contrary data to our attention. However, in the paper by Payne *et al* (ref 1 above) comparing sputum, bronchial aspirate, and needle biopsy and bronchoscopic forceps biopsy specimens discrepancies between the results of these procedures and diagnosis based on eventual surgical biopsy were also common in large cell carcinoma. The explanation for their better overall agreement between bronchial biopsy and eventual tissue diagnosis may be the marked difference in the type of carcinomas in the two series. Their series was heavily weighted in favour of squamous cell carcinoma, while this cell type comprised only one quarter of our group.

While Rudd *et al* have reported comparable degrees of accuracy with fiberoptic bronchoscopy and rigid bronchoscopy (ref 2 above) their comparison is not relevant to our study. Indeed, most of the carcinomas we encountered were peripheral, well beyond the visibility of the flexible instrument, and were biopsied under fluoroscopic control. Biopsy via the rigid bronchoscope would have been impossible.

Finally, we agree that multiple biopsy specimens and operator experience will enhance results. In more than 5000 fiberoptic bronchoscopies since 1973, we have routinely obtained three to five biopsy specimens unless brisk bleeding is encountered. It is of interest that with their multiple biopsy sample technique Gellert *et al* (ref 3 above) have reported only 78.6% of positive biopsies in cases of *visible* carcinoma, a number considerably less than the 94.9% we have achieved.<sup>1</sup>

It is clear from the above comments that factors other than the "skill of the bronchoscopists and pathologists concerned" are responsible for the disagreement observed by us between bronchoscopic biopsy diagnosis and eventual diagnosis. There is one other factor which may affect the results obtained—namely, the degree of objectivity applied in reading the histologic preparations. We suspect strongly that our total commitment to objective reading of the histological preparations contributed to the greater difference in cell type between biopsy and final diagnosis reported by us.

We believe that the important message of our paper is valid—that is, the physician must be cautious when planning treatment based on lung cancer cell types obtained from small biopsy specimens.

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<sup>1</sup> Teirstein AS, Chuang MT, Miller A, Choy AR, Nieburgs HE. Flexible bronchoscopy in nonvisualized carcinoma of the lung. *Ann Otol Rhinol Laryngol* 1978;87:318–21.

#### Dysphonia caused by inhaled steroids: recognition of a characteristic laryngeal abnormality

SIR,—The conclusion by Dr Alan J Williams and his colleagues (November 1983;38:813–21) that inhaled corticosteroid was the cause of the vocal cord abnormality might have been better supported had the authors provided evidence that similar quantities of propellant, etc, had been inhaled as a result of the increased use of  $\beta$  stimulant or ipratropium once patients had discontinued inhaled corticosteroids. In the studies by the British Thoracic and Tuberculosis Association dysphonia was found in 3–9% of patients, both in those receiving placebo inhaler and in those receiving inhaled corticosteroids.<sup>1,2</sup> One still has to consider the case against inhaled steroids as "not proven."

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<sup>1</sup> British Thoracic and Tuberculosis Association. Inhaled corticosteroids compared with oral prednisone in patients starting long-term corticosteroid therapy for asthma. *Lancet* 1975;ii:469.

<sup>2</sup> British Thoracic and Tuberculosis Association. A controlled trial of inhaled corticosteroids in patients receiving prednisone tablets for asthma. *Br J Dis Chest* 1976;70:95.

\*\* This letter was sent to the authors, who reply below.

SIR,—In evaluating the effect on dysphonia of stopping aerosol steroid we recognised that it was important to ensure that the total propellant intake was not decreased. Hence, as described in our report, the decrease in propellant intake due to cessation of aerosol steroid was matched by an increase due to additional inhaled bronchodilator. Indeed, in some of the patients the total propellant intake was actually greater after the aerosol steroid was discontinued. Furthermore, two of our patients were taking inhaled therapy exclusively as dry powder preparations containing a lactose base but no hydrocarbon propellant. Since completing the reported studies we have seen further cases in this latter category.

It is of interest that in the BTTA studies of inhaled corticosteroid in asthma hoarseness was volunteered in some 9% of patients in both the placebo and the inhaled steroid groups. However, no formal assessment of the symptoms was undertaken (speech analysis, laryngoscopy, time course and duration of symptoms) so that we do not know how many of these patients had vocal cord deformity and how many had hoarseness due to other common causes such as candidiasis, viral infection, or psychogenic factors. Double blind comparison of aerosol steroid and placebo (with the same propellant intake) in a study designed to evaluate dysphonia<sup>1</sup> showed that this symptom was five times as common with aerosol steroid as with placebo.

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<sup>1</sup> Toogood JH, Jennings BA, Greenway RW, *et al*. Candidiasis and dysphonia complicating beclomethasone treatment of asthma. *J Allergy Clin Immunol* 1980;65:145–53.

## Correction

### The secretory IgA system of lung secretions in chronic obstructive bronchitis

In the paper by J Wiggins *et al* (July 1984, pp 517–23) the formula on p 519, col 1, should have a plus instead of a minus sign in the denominator. It should read:

$$t = \frac{CV_1 - CV_2}{\sqrt{\frac{CV_1}{2n_1} + \frac{CV_2}{2n_2}}}$$