Pulmonary 'hamartomata'

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Pulmonary hamartomata are rare, and angiomatous and chondromatous varieties are those usually encountered. The angiomatous or vascular pulmonary hamartoma is often part of the recognized hamartomatous syndrome, multiple hereditary haemorrhagic telangiectasis (Rendu-Osler-Weber disease), and satisfies all the criteria of a true hamartoma. The claim of the chondromatous lesions to be classified as hamartomata is tenuous, and these are now more generally accepted as mixed tumours, styled chondro-adenomata, exactly comparable with mammary fibro-adenomata, which are usually benign, and which appear in adult life and exhibit growth when the parent organ is mature, and occasionally malignant change. True epithelial pulmonary hamartomata have been described (Harris and Schattenberg, 1942; Jones, 1949; Thomas, 1949) but nearly always in premature or stillborn infants. Rare fibroleiomyomatous pulmonary hamartomata alone or as part of the disease of tuberous sclerosis (epiloia) also occur (Dawson, 1954), and the very occasional pulmonary blastoma (embryoma) may possibly qualify as a hamartoma. While tumours of nerve sheath origin are occasionally found in the lungs, and mediastinal neural tumours may be found in patients with the true hamartomatous syndrome of neurofibromatosis (von Recklinghausen's disease), no report of pulmonary neural tumours in a patient with neurofibromatosis has been found.

The term 'hamartoma' was introduced by Albrecht in 1904 and is applied to developmental tumour-like malformations in which the normal components of an organ are abnormally represented, in their quality, arrangement, degree of differentiation, or all three. The term is not applicable to tumours acquired after the parent tissue has attained structural maturity. While a hamartoma is essentially a malformation and not a tumour, none of its component parts is assured against neoplastic change, and to cover this eventuality the less familiar term 'hamartoblastoma' was coined, also by Albrecht. And although hamartomata are developmental malformations, growth does not necessarily cease with maturity

of the parent organ, and malignant change may occur in adult life, for example, in the bony excrescences of diaphyseal aclasis. Thus the term hamartoma, while convenient and attractive, is easily abused, and the evidences adduced for the inclusion of individual abnormalities as hamartomata are often more philosophical than scientific.

The purposes of this paper are to state the incidence of the more common varieties of pulmonary 'hamartoma' in relation to other pulmonary tumours, to describe the features, clinical, radiographic and operative, of these lesions, and to justify the surgical approach to the chondromatous variety, since these so rarely endanger the patient. During the period when eight vascular and 27 chondromatous lesions were managed, one pulmonary fibroleiomyoma was resected.

PULMONARY ARTERIO-VENOUS FISTULA This is the term generally applied to the vascular pulmonary hamartoma. During development the opportunity is presented for a persistence of abnormal communications between the arteries and the veins, since these arise from a common capillary plexus. Pulmonary arterio-venous fistulae probably result from incomplete fusion of venous and arterial septa, or from the disintegration of hypoplastic septa in the face of normal or abnormal stresses such as coughing or mitral stenosis. The relationship between anatomical arterio-venous shunts in the lungs and pathological arterio-venous fistulae is conjectural, but the latter develop on a background of generalized congenital vascular hypoplasia. The essential lesion in clinically significant pulmonary arterio-venous fistulae is a more or less direct communication between afferent and efferent vessels which creates a right-to-left extracardiac shunt that bypasses the pulmonary capillary bed and returns unoxygenated blood to the systemic circulation. As a result of the shunt there is an increase in blood volume and peripheral vascular dilatation which, with arterial oxygen unsaturation, account for the clinical features of cyanosis, finger-clubbing, polycythaemia, an extracardiac murmur, and dyspnoea, which is unim-

pressive in relation to cyanosis. Unlike systemic arterio-venous fistulae, which decrease total systemic resistance and therefore increase the work of the heart, pulmonary arterio-venous fistulae are only rarely associated with cardiomegaly, since the vascular resistance of the lungs is normally so low that the presence of a shunt in parallel within the lungs does not materially alter the overall vascular resistance.

During the 10-year period 1950–59, when 3,000 patients with bronchial carcinoma and 40 patients with bronchial adenoma were seen in the Regional Thoracic Unit in Edinburgh, eight patients with pulmonary arterio-venous fistulae were managed. The Unit serves a relatively static population of one and a half million, and these figures are believed to represent the incidence of the lesions mentioned in this population. Six of these eight cases have previously been described in detail (le Roux, 1959) together with the natural history of the disease.

William Hunter (1762) was the first to describe a systemic arterio-venous fistula, the consequence of injury to the brachial vessels during blood-letting. Churton's (1897) was the first description of the pathology of pulmonary arterio-venous fistulae; the first ante-mortem diagnosis of the lesion was made by Smith and Horton (1939), and a pulmonary arterio-venous fistula was first resected by Shenstone (1942). Since then more than 300 cases have been reported.

Patients with pulmonary arterio-venous fistulae present because of symptoms, earlier enumerated, because of an abnormality found on a chest radiograph made for an unrelated purpose, or with complications such as haemorrhage, infection or a cerebral lesion. As in the patient with cyanotic heart disease, so with pulmonary arterio-venous fistulae, polycythaemia and arterial oxygen undersaturation predispose to cerebral thrombosis, and infection is likely in the related area of encephalomalacia with the formation of brain abscess. The pulmonary vascular shunt is said to offer a leak through the normal pulmonary filter, so that pathogenic organisms are more likely to reach the systemic circulation, but the normal lung must be a very inadequate filter.

The fistulae may occur anywhere in the lungs but are most common in the lower lobes, particularly in the right ; in 20% of patients the lesions are multiple, and in half of these they are bilateral. A family history is not uncommon, and there is a well-recognized hereditary tendency. There is a family history of multiple hereditary haemorrhagic telangiectasis in 15% of cases, and in 40% there are telangiectases elsewhere. The lesions are found at any age, in either sex, and in all races. The typical pulmonary arterio-venous fistula casts a radiographic shadow that is rounded or lobulated, is homogeneous, lies within the pulmonary parenchyma but may abut on the pleura, has well-defined margins, and is bound to the pulmonary hilum by cord-like extensions which are the shadows of dilated subserving vessels. As a preliminary to surgical management, angiocardiography is essential so that all fistulae may be recognized and none left unresected. Management in patients suitable in other respects for thoracotomy is by resection because this is the only way in which the fistulae can be closed, and, in the absence of closure, mortality which is directly the consequence of the pulmonary abnormality is close to 50% (Muri, 1955). The treatment of choice is the most limited resection possible because of the likelihood of multiplicity of fistulae and the possibility of the development of further fistulae. Lobectomy should rarely be necessary ; it is often possible to manage the fistula by segmental resection, and in most cases the fistula, part of which is usually covered only by pleura, can be stripped from the lung after the ligation of feeding and draining vessels without the sacrifice of any pulmonary tissue. The afferent and efferent vessels are usually dilated pulmonary arteries and veins, but occasional examples are found in which the afferent supply is wholly or partly systemic, from bronchial or intercostal arteries or from abnormal aortic branches. Where a fistula is subjected to systemic pressure the complication of haemorrhage is more likely.

The chest radiographs and angiocardiographs of a typical case of right lower lobar pulmonary arterio-venous fistula are shown (Figs. 1 and 2).

CHONDROMATOUS PULMONARY 'HAMARTOMA' (PULMONARY CHONDRO-ADENOMA) The inclusion of this lesion among the hamartomata is habitual rather than reasoned and objectionable on at least two counts: because (1) these tumours do not fulfil the criteria of hamartomata, and (2) not only is cartilage not their only component but it may in occasional examples be absent. The term 'chondromatous hamartoma' is, however, so deeply ingrained that it will certainly continue to be used, at least by the present generation of thoracic surgeons and respiratory physicians, and none of the alternative names is completely satisfactory. These lesions have been defined by Willis (1958) as, and are probably best called, mixed tumours of the bronchial wall, in which proliferation of bronchial epithelium is accompanied by proliferation of underlying mesenchymal tissues. Their
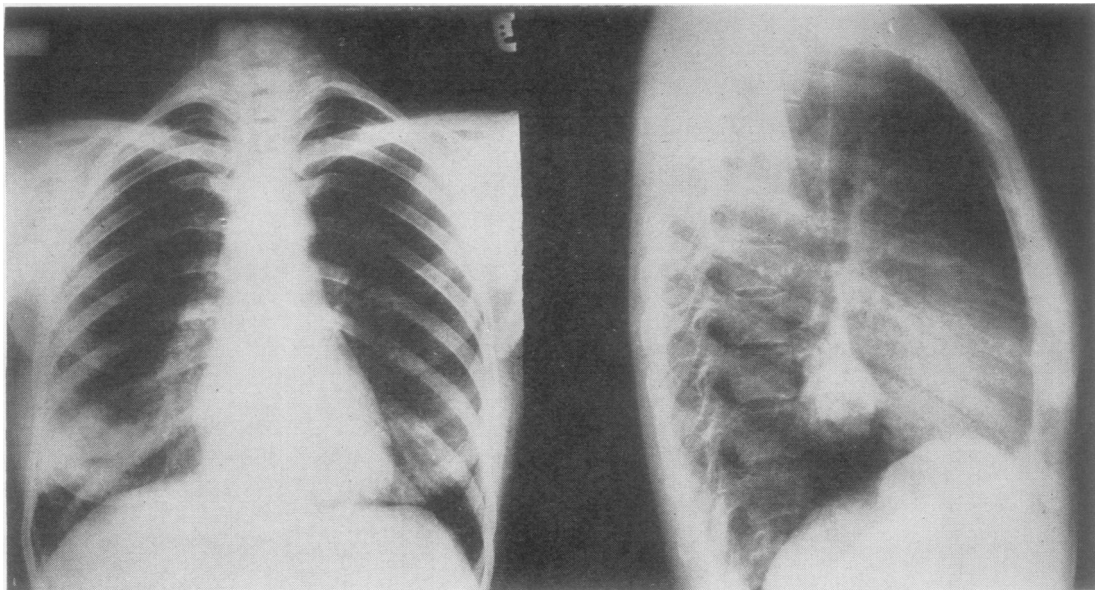
FIG. 1.   *Postero-anterior and right lateral chest radiographs showing a pulmonary arterio-venous fistula in the right lower lobe.*
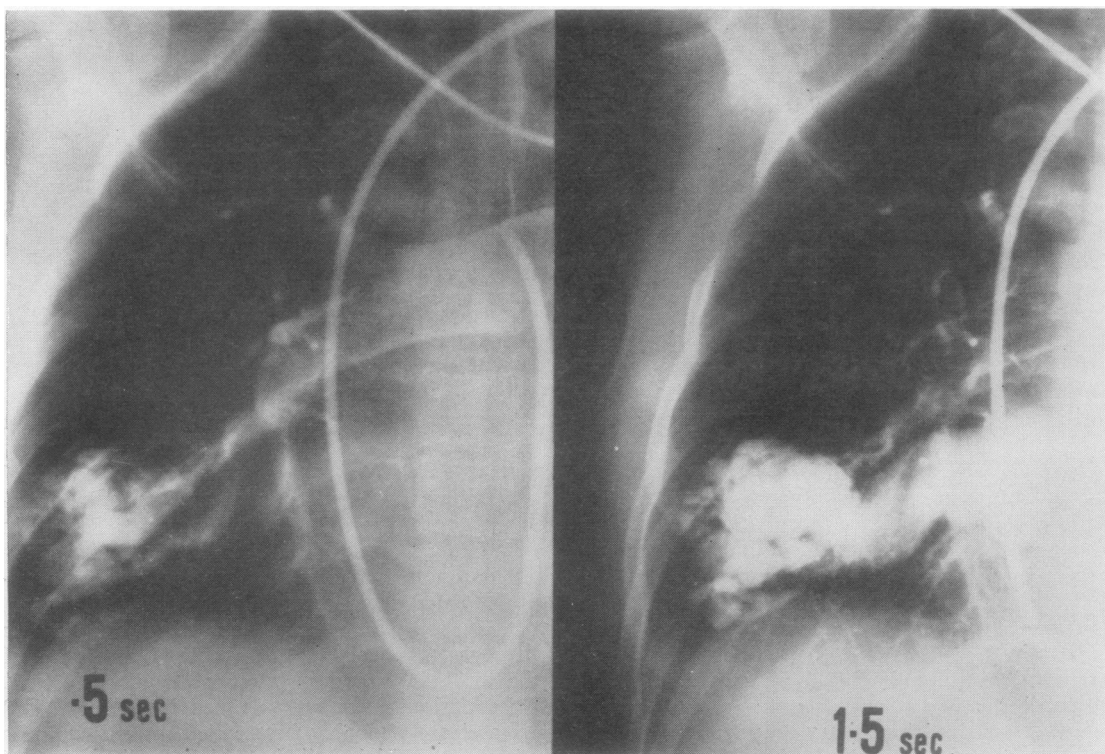

FIG. 2.   *A right pulmonary arterial angiogram in which the fistula shown in Fig. 1 is outlined. The enormous draining vein is well shown in the film made 1·5 seconds after the injection of dye.*

mode of growth is papillary or polypoidal, like that of mammary fibro-adenomata with which they are exactly comparable.

The lesion, which may on rare occasions be multiple, was first recorded by Lebert (1845), and Goldsworthy (1934) suggested that 'hamartoma chondromatosum pulmonis' was a proper designation. Scarff and Gowar (1944) reported an example of this tumour which was devoid of cartilage, and this they called a pulmonary fibro-adenoma. A further example recorded by Brewin (1952) contained much fatty tissue, and he called this a pulmonary lipochondro-adenoma. Brewer, Brookes, and Valteris (1953) designated the whole group of tumours adeno-chondromata, but Adams (1957) preferred the term 'chondro-adenoma' to distinguish these tumours from ossifying adeno-chondromata which he and others (Thomas and Morgan, 1958) classify with pulmonary adenomata. Chondromatous hamartomata are said to be found in the lungs in 0·25% of necropsies (McDonald, Harrington, and Clagett, 1945), and similar chondromatous tumours are found in horses and cattle (Spencer, 1962).

During the 10-year period 1950–59, when 3,000 patients with pulmonary carcinoma and 40 with bronchial adenoma were managed in Edinburgh, 27 patients with chondromatous hamartomata were treated, and in two others the diagnosis of a chondromatous lesion was made on radiographic evidence but not substantiated histologically because of the age and frailty of the patients. No further reference will be made to these two patients, a man and a woman both in the eighth decade. In two of the 27 treated patients the tumours were endobronchial, and in the others they lay peripherally in pulmonary parenchyma. Nineteen of the 27 were men: a greater incidence among men is reflected in all other series and the preponderance varies from 2 to 3:1 (Stein and Poppel, 1955 ; Jackson, McDonald, and Clagett, 1956). The youngest patient was 30 and the oldest 64 years. In a series of 107 cases reviewed by Jones (1949), the age range was 21–78 years, and in a series of 48 reported by Willis (1948) the range was 28–74 years. Perry (1959) reported an example in a boy of 16, the youngest recorded case ; the age range thus makes it very unlikely that the lesion is a congenital malformation.

None of the 25 patients with peripheral pulmonary opacities treated in Edinburgh presented because of symptoms ; all were investigated because of the finding of a well-circumscribed pulmonary shadow at routine chest radiography for unrelated purposes. The two patients with endobronchial tumours presented with symptoms of bronchial obstruction. In one the tumour lay in the right main bronchus and in the other in the left upper bronchus. The tumour in the right main bronchus was resected at bronchoscopy and has not recurred during 13 years of observation ; that in the left upper bronchus was managed by bronchotomy.

Of the 25 peripheral lesions, 19 were right-sided (six in the upper lobe, seven in the middle, and six in the lower lobe) and six were left-sided (four in the upper lobe and two in the lower lobe). The tumours can clearly occur anywhere in the lung, but from reported examples occurrence in one or other lower lobe appears a little more common than elsewhere in the lung (Perry, 1959).

Of the 25 peripheral lesions, 13 were managed by enucleation without loss to the patient of any pulmonary tissue, eight by lobectomy, and four by segmental resection. In 23 cases there was no previous chest radiograph with which to make comparison ; in these, three of the tumours measured 1 cm. in greatest diameter, 19 measured from 1 to 3 cm., and one measured 6 cm. In two patients there was unequivocal radiographic evidence of tumour growth, in one over a six-year period an increase from 2 to 3 cm. in diameter (Figs. 3 and 4) and in the other over a two-year period an increase from 1·5 to 2·2 cm. In nine cases calcium could not be recognized within the radiographic opacity even with the help of tomography ; in 12 there was a single speck of calcium within the shadow of the tumour ; and in four there was scattered punctate calcium throughout the lesion (Fig. 5). In the many reported examples of pulmonary chondro-adenoma, the size has varied from a few millimetres to a mass that has filled the hemithorax and bulged the intercostal spaces (Good and Wilson, 1958). The majority of lesions have been less than 5 cm. in diameter, usually between 1 and 3 cm. Jackson *et al.* (1956) quote examples of tumours 10 cm. in diameter and of one that weighed 12 lb. (5·44 kg.). These authors describe two massive cystic lesions, which they believe may be examples of the same variety of tumour, and Adams (1957) reported a case in which the lesion was cavitated.

Growth of pulmonary chondro-adenomata, as shown by an increase in size on serial chest radiographs, has been observed surprisingly often (Adams, 1957 ; Jensen and Schiødt, 1958 ; Perry, 1959), surprisingly because it is in most clinics standard practice to resect on sight peripheral spherical pulmonary lesions in patients who are symptomless and in whom there is neither certain evidence of the benignity of the lesion responsible for the radiographic shadow nor a contra-indica-
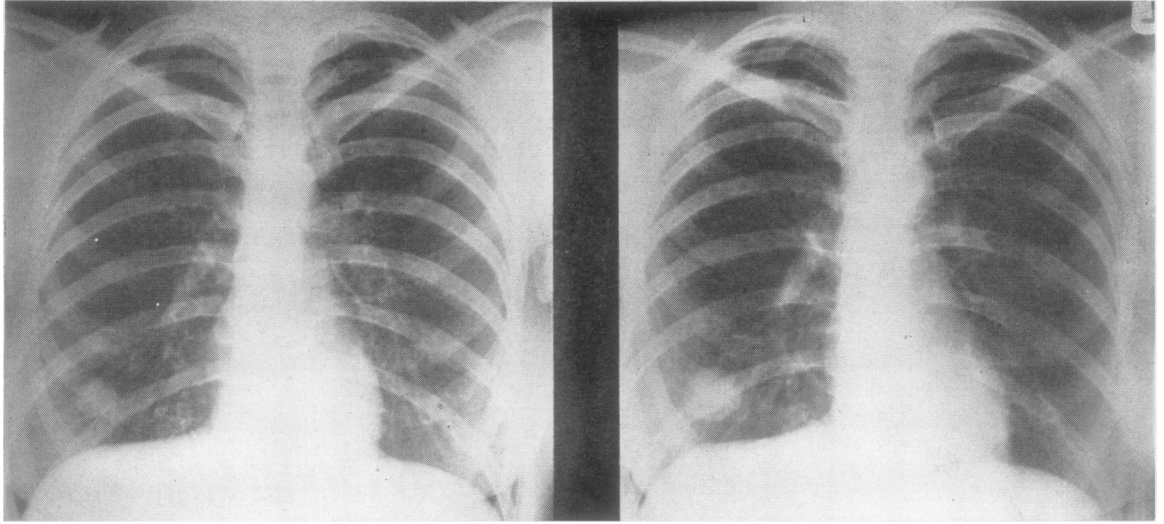
FIG. 3.   *Growth in a pulmonary chondro-adenoma is seen in these chest radiographs made at an interval of six years.*
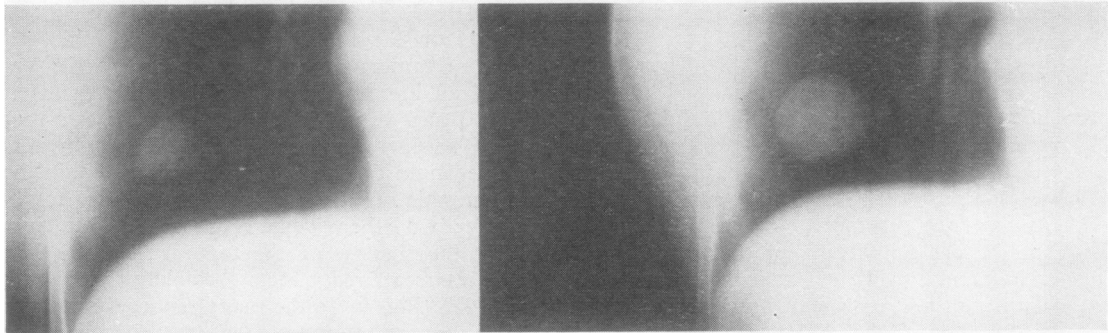

FIG. 4.   *Tnese tomographic cuts correspond with the P.A. chest radiographs shown as Fig. 3. There is no visible calcification.*

tion to thoracotomy. With this Lady Macbeth or 'out damned spot' principle some, for example, Garland (1960), are in disagreement, but it remains unusual for a lesion to be observed over several years and be seen steadily to increase in size and yet not to submit to exploratory thoracotomy the patient who harbours such a lesion. The rate of growth of pulmonary chondro-adenomata is slow, and observation for two or three years is usually reported before radiographic evidence of an increase in size is unequivocal. Jensen and Schiødt (1958) observed a hamartoma to double in size over 23 months, and there are reports of these lesions achieving a size of 1 cm. within a year of a chest radiograph having been reported to be normal but without the opportunity of restrospective scrutiny of such 'normal' films. When the diameter of a spherical lesion has, by measurement, doubled on a plain film, it must

be remembered that its volume has increased eightfold.

A differentiation between benign and malignant pulmonary nodules by rate of growth has been attempted (Nathan, Collins, and Adams, 1962). Nearly all solitary malignant nodules double in size within 40 weeks whereas benign nodules rarely double in size in less than 70 weeks. In patients under 40 years of age, tumours grow quickly, so that a rapid doubling time (of under five weeks) may be found in malignant tumours in the young. Such a rapid increase in size is rare in primary pulmonary tumours in patients over the age of 40, and a rapid doubling time in a solitary pulmonary shadow in the aged is thus more strongly suggestive of an inflammatory lesion than of a malignant tumour. But these measurements of time are retrospective and represent only average behaviour. Deliberate observa-

FIG. 5. *Punctate calcification in a pulmonary chondro-adenoma is well seen in the tomograph superimposed on the P.A. chest radiograph.*
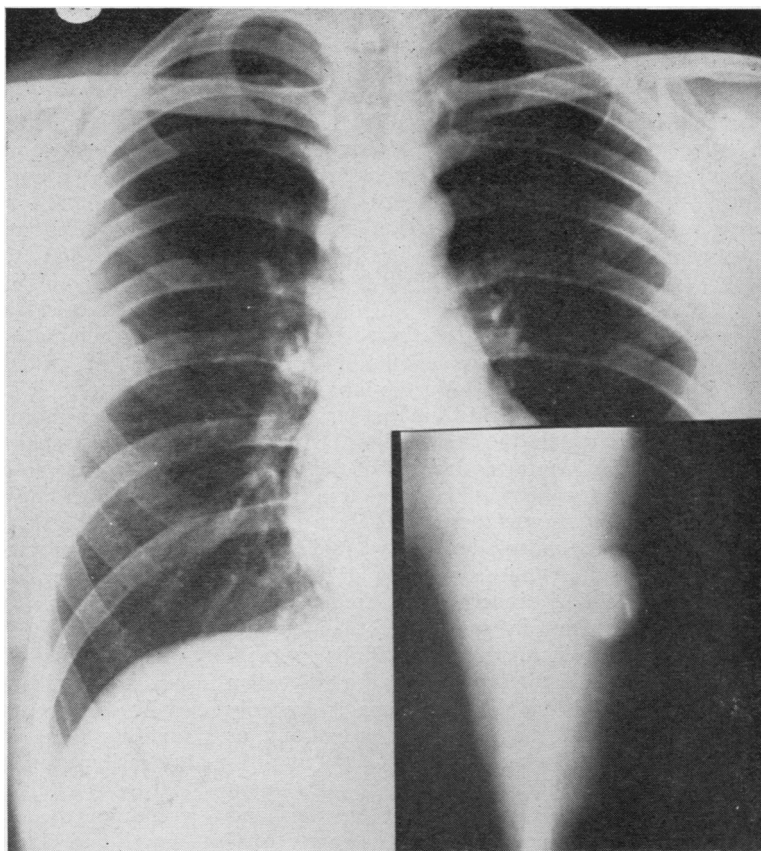
tion to allow of the application of growth-rate formulae in the making of a diagnosis in a patient with a solitary pulmonary shadow is, for the individual patient, unacceptably hazardous. The 'inevitable' delays between out-patient examination, admission for detailed investigation, and submission to thoracotomy are such that a series of films becomes available for comparison to allow of the recognition of quickly changing inflammatory lesions, and a very small number of patients are submitted to thoracotomy for a lesion that would have healed spontaneously. In Edinburgh, in the decade mentioned earlier, there were fewer than 1% in over 500 thoracotomies for pulmonary lesions, the diagnosis of which was uncertain before operation. The need for management by observation may be thrust upon the physician or surgeon ; the patient may be unsuitable for thoracotomy for unrelated reasons, or may decline operation, and in these circumstances the opportunity for observation is valuable in providing evidence of the natural history of solitary pulmonary nodules. There are reasons other than the danger to the patient of not resecting a malignant nodule that make management by observation unacceptable: repeated observation will prove irksome for the patient who may default or become introspective and psychologically disturbed, and the presence of an unexplained and abnormal shadow may be a bar to employment, emigration, or life insurance. In respect of the growth rate of bronchial carcinoma, Rigler (1957) has shown how common it is for a radiographic pulmonary abnormality to precede symptoms by as long as two years, for such an opacity to increase and regress rapidly when an evanescent inflammatory lesion complicates the tumour, and for a bronchial carcinoma to grow slowly, over eight or nine years, without treatment before ultimately causing death.

Tracheo-bronchial chondromata occur in the ratio of about one to every 20 or 30 peripheral chondromatous tumours. Perry (1959) has recorded an example of a chondro-adenoma in

the trachea ; most occur in the major bronchi. Paterson (1956) added one example to a review of 29 previously recorded cases. The histological similarity between pulmonary and tracheo-bronchial chondromata was shown by Sutherland, Aylwin, and Brewin (1953). Management by bronchotomy is probably preferable to management by endo-bronchial resection through a bronchoscope. Pulmonary resection is necessary only when bronchial obstruction has been of such long standing that subtended lung is irreversibly damaged.

The macroscopic features of the common peripheral pulmonary chondra-adenoma, 1 to 3 cm. in diameter, are mobility within the lung, smoothness and lobulation of the tumour surface, and the ease with which the lesion can be cleanly ejected from the lung after incision of the visceral pleura. Mammary fibro-adenomata are, because of their mobility, sometimes called breast mice, and pulmonary chondro-adenomata could equally well be called lung mice so easily do they slip through examining fingers. The frequency of management by enucleation rather than by segmental resection increases with familiarity with the lesion, and lobectomy is undertaken only when the diagnosis of bronchial carcinoma is the only one entertained at the time of thoracotomy or when the lesion is large.

Histologically, pulmonary chondro-adenomata show areas of fibro-cartilage, often calcified and occasionally containing metaplastic bone, separated by cleft-like spaces lined by bronchial epithelium (columnar, cuboidal, or occasionally ciliated), and so versatile is the mesenchymal element of these tumours in its capacity for differentiation that mucoid, adipose, fibrous, and lymphocytic elements and smooth muscle may all be found in the same tumour.

Malignant change in pulmonary chondro-adenomata has occasionally been recorded (Greenspan, 1933 ; Simon and Ballon, 1947 ; Sedlezky, 1955 ; Kuyjer, 1955 ; Klepser, 1956 ; and Effler, 1951). In any attempt to estimate the natural history of a malignant tumour from the scrutiny of histological sections, the evidence of the initial lesion having been a chondro-adenoma must at best be circumstantial and always a little suspect, but, however rare malignant change may be in these tumours, there is no reason why it should not occur. In mammary fibro-adenomata, malignant change involves the connective tissue component, and the malignant tumour is therefore a sarcoma. Carcinoma may invade or co-exist with mammary fibro-adenoma, but carcinomatous change in a fibro-adenoma, if it occurs, must be

extremely rare. Pulmonary carcinoma is so common a lesion that its co-existence with and invasion of a chondro-adenoma must occur, and some examples of pulmonary ˙sarcoma may have had their origin in the connective tissue elements of a chondro-adenoma.

While it is not possible on radiographic grounds alone to make a certain diagnosis of pulmonary chondro-adenoma, there are some radiographic features that together suggest the diagnosis: clarity of outline, small size, and the presence of punctate calcification. Calcification in relation to a tuberculoma is more often circumferential and laminated, and satellite shadows related to a pulmonary nodule make the diagnosis of a tuberculous lesion more likely. While size alone is of no value in reaching a diagnosis in the individual patient, several pertinent observations have been made regarding the size of solitary pulmonary lesions. The threshold of visibility of pulmonary shadows varies with the experience of the observer, with radiographic technique, with the shape and outline of the opacity, and perhaps with the size of the radiographic film used. Small single shadows are more easily missed than are small multiple shadows ; miliary shadows (2 mm. or less) are easily seen because of their multiplicity. Nipple shadows range in diameter from 5 to 15 mm. and are easily recognized, but they are usually bilateral and lie at a fairly constant level in relation to the domes of the diaphragm. Using lucite markers, Newell and Garneau (1951) have measured accurately the size and shape of this material which casts a recognizable radiographic shadow through the full thickness of the chest, and single shadows of less than 5 mm. are recognized only rarely and with difficulty. Good and Wilson (1958) reviewed over 700 peripheral shadows, of which 7% (52) were less than 1 cm. in diameter. Roughly one out of every six of those less than 1 cm. in diameter contained calcium. In only two patients in their series was a lesion, the radiographic shadow of which was less than 1 cm. in diameter, resected, and in both these patients the lesion was a metastasis. Taylor, Rivkin, and Salyer (1958) reviewed 236 peripheral opacities, and of the carcinomata none was less than 1·5 cm. in diameter. A single pulmono-pulmonary metastasis from bronchial carcinoma less than 1 cm. in diameter has been recognized on at least five occasions in Edinburgh, but here attention has been drawn to the metastasis by the obvious primary tumour. Multiple pulmonary metastases from bronchial carcinoma, all of them less than 5 mm. in diameter, have also been recognized. There is therefore nothing about the physical properties of bronchial carci-

noma which makes this unrecognizable radiographically until it has achieved a diameter greater, say, than 5 to 8 mm. Rigler (1957) has observed cavitation in small carcinomata (1 to 1·5 cm.) and has later seen the cavity disappear and the lesion revert radiographically to a solid mass. Davis, Peabody, and Katz (1956) reviewed more than 1,200 solitary circumscribed nodules less than 6 cm. in diameter in which there was no evidence of calcification or of cavitation. Of these, 36·7% were malignant tumours, 41·6% were granulomatous lesions including those of tuberculosis, and 8·5% (100 cases) were 'hamartomata'. In this series, three examples of bronchial carcinoma 1 cm. 'or less' in diameter were detected. These authors agree that while observations of size, sharpness, and regularity of margin, density, recent origin, rate of growth, and the presence of calcification are often of value in making a provisional diagnosis, this diagnosis remains in the individual patient only an educated guess on which it is unsafe to base management by observation. Calcification has been observed in small carcinomata, and carcinoma may develop within or in close proximity to a healed tuberculous focus in which there is calcium.

Finally, peripheral, well-circumscribed, and roughly circular shadows seen on plain chest radiographs are often called 'coin' lesions because they resemble a coin. This term is doubly inappropriate: the lesions are spherical, not flat, and management is most often debatable when the lesion is small and therefore almost invariably smaller than any coin in circulation. Since coinage is debased there is no economic reason for making small coins and few measure less than 2 cm. in diameter. In Great Britain the smallest coin in circulation is the 6d. piece, which measures 2 cm. in diameter, and the small 'silver' 3d. piece occasionally encountered measures 1·5 cm. in diameter.

SUMMARY

Pulmonary vascular hamartomata (pulmonary arterio-venous fistulae) are rare. They are true hamartomata and are amenable only to surgical excision. This is the management of choice unless the lesions are multiple and widespread, because these hamartomata endanger the patient's life. Chondromatous pulmonary 'hamartomata' do not fulfil any of the criteria of hamartomata. They are mixed tumours of the bronchial wall which only rarely give rise to symptoms—when they produce bronchial obstruction. They grow slowly and can only very occasionally endanger the patient; but since they are usually indistinguishable, even when small, from malignant pulmonary tumours they demand surgical resection. This is usually possible by simple enucleation.

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