Morphology and pathogenesis of desquamative interstitial pneumonitis[1]

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Valdivia, E., Hensley, G., Wu, Jane, Leroy, E. P., and Jaeschke, W. (1977). *Thorax*, **32**,
7–18. **Morphology and pathogenesis of desquamative interstitial pneumonitis.** Thirty human
lung biopsy specimens have been diagnosed as desquamative interstitial pneumonitis. Six cases
had intraalveolar lesions, believed to be early, while 20 had advanced disease characterised
by intraalveolar cellular clumps, alveolar wall fibrosis, distortion, and loss of pulmonary
parenchyma. Electron microscopy, high resolution light microscopy, and cytological
examination have shown that the characteristic clumps in the alveolar air spaces are formed
predominantly by enlarged and aggregated macrophages. Lymphocytes and eosinophils are also
present in the intraalveolar clumps and in alveolar walls. Inflammation and immunological
mechanisms are suggested as causes of the cellular clumping. Interstitial pneumonitis, alveolar
wall fibrosis, changes in the alveolar epithelium, and loss of lung parenchyma are believed to
be secondary events.

Desquamative interstitial pneumonitis (DIP) be-
longs to a poorly understood group of chronic
pulmonary lesions which need lung biopsy for
diagnosis. The original series was collected mostly
from consultations by Liebow *et al.* (1965), who
established clinical, radiological, and morpho-
logical patterns which they believed to be specific
for a human disease responsive to steroid treat-
ment. Since then similar cases have been reported
describing light and electron microscopy features
which confirm the original description (Gaensler
et al., 1966; Goff *et al.*, 1967; Klocke *et al.*, 1967;
Scadding and Hinson, 1967; Leroy, 1969; Short-
land *et al.*, 1969; Farr *et al.*, 1970; Scadding, 1970;
Bates *et al.*, 1971; Gould *et al.*, 1971; McNary
and Gaensler, 1971; Patchefsky *et al.*, 1971;
Corrin and Price, 1972; Patchefsky *et al.*, 1973a;
Patchefsky *et al.*, 1973b; Rhodes, 1973; McCann
and Brewer, 1974). A controversial feature is the
identification and origin of the cells found in
the alveolar spaces since Liebow *et al.* (1965)
favoured a primary exfoliation of type II granular
pneumocytes, epithelial cells with late or second-
ary presence of alveolar macrophages. Scadding

and Hinson (1967), Scadding (1970), and
Patchefsky *et al.* (1971, 1973a, b) believe that
desquamative interstitial pneumonitis is only a
temporary or microscopic variation of chronic
interstitial pneumonitis which may have mural
or exfoliative types of inflammatory reaction. The
pathogenesis of the DIP lesions is obscure; a
viral origin has been suggested by Liebow *et al.*
(1965) and investigated by McNary and Gaensler
(1971) while a hypersensitivity mechanism has
been proposed by several authors such as Liebow
et al. (1965), Gaensler *et al.* (1966), and Leroy
(1969).

The present study describes the morphological
features of 30 cases which show that there may
be early, intermediate, and late stages of the
disease. Furthermore, the availability of resin-
embedded material permits examination at high-
resolution light microscopy and with the electron
microscope. The presence of eosinophils in the
early and chronic phase, abundance of macro-
phages, and lymphocytes suggest that the cellular
reaction observed in these cases is a form of lung
injury with features characteristic of an altered
inflammatory response. The main objectives of
this article are: (a) to describe and define the

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morphological lesions in the lung and to identify the cellular components observed in the desquamative exudate; (b) to propose a differentiation between early and late stages of the disease; and (c) to offer interpretations related to the pathogenesis of DIP.

Material and methods

Thirty lung specimens were obtained by biopsy in our institutions or microscopic slides were reviewed for consultation. Three necropsies, including case number 15 of Liebow's (1965) series, provided abundant pulmonary tissue since the diagnosis was made by biopsy before death. All cases were reviewed by at least three pathologists, one of them an outside consultant, using light microscopy of paraffin-embedded material with the following stains: haematoxylin-eosin, PAS, toluidine blue, Prussian blue, osmic acid for fat, elastica, Gridley, acid fast, and trichrome (Armed Forces Institute of Pathology, 1960). The lung specimens in 18 cases were divided for frozen storage for immunofluorescence, bacteriology, virology, acid-fast bacilli, fungus cultures, frozen section, and formalin fixation, and small cubes were fixed in phosphate buffered 2·75% glutaraldehyde and Millonig's fixative (Pease, 1964). The glutaraldehyde fixation was followed by one hour's staining in Millonig's fluid. Some of the specimens were processed including staining in block with uranyl acetate in the 25% ethanol dehydrating agent (Pease, 1964). Embedding was in epon-araldite. The lung specimens were trimmed, preserving the pleura or small bronchi. The surface size of the specimens varied from 2 to 16 mm². One-micron sections were cut with the Porter Blum M3 or LKB ultramicrotomes and stained with alkaline 1% toluidine blue, and the slides were mounted in epon-araldite. Electron microscopy was done on a RCA EMU3G instrument. Cytological details were obtained by making tissue imprints, the slides being fixed immediately after biopsy with ethanol-ether, methanol, or air dried. Stains of imprints were H and E, PAS, methyl green pyronin, Giemsa, and Wright (Armed Forces Institute of Pathology, 1960). One biopsy was obtained by the transbronchial technique described by Andersen and Fontana (1972).

Results

GENERAL CONSIDERATIONS
All patients were adults and had a clinical diagno-

sis of idiopathic interstitial pneumonitis. Three patients were asymptomatic but pulmonary lesions were observed by radiographic examination; all others had respiratory symptoms and radiographic evidence of interstitial pulmonary fibrosis. Frequently the disease started insidiously with cough, dyspnoea, clubbing, loss of weight, and a progressive course. A few patients began their illness more rapidly with fever and apparent pneumonic episodes. The material examined in this study included biopsies from the left lung in the area of the lingula or tip of lung lobes, since for technical reasons surgeons preferred to follow a limited thoracotomy when the lung was believed to be uniformly involved. Twelve cases had limited clinical and operative information since only microscopic slides and referral data were available. Seven cases were studied serologically for virus infection and the lung specimens were inoculated in different cell strains of tissue culture and observed for 30 days, producing negative results. The same number of bacteriological and fungus cultures from the lung tissue had yielded no growth. Immunofluorescence studies included nonspecific demonstration of immunoglobulins in four cases. Two biopsies showed positive reactions for immunoglobulins and complement in the mononuclear cells of the clump which also reacted with antisera to pigeon and thermophylic Actinomyces antigens. Both cases also showed alveolar macrophage cells containing phagocytised eosinophils in their cytoplasm and immunofluorescence evidence of fibrin fragments in the alveolar spaces.

GROSS FEATURES
The gross involvement of the lung was presumed to be generalised since the sampling was limited and permitted only restricted examination. In 16 cases, lung induration was described presenting either fine nodularity or patchy lesions. The visualised lung in cases 3 to 5 presented foci of consolidation measuring an average of 0·6 cm. The pleural vessels were conspicuous, engorged, and dilated, and the serosa was slightly thicker than normal. The lung in cases 7 to 30 presented pleural fibrosis; case 10 had a shell of calcification which was nodular and extensive. Two cases had a cobblestone appearance, the protruding nodules measuring approximately 0·8 cm in diameter. Case 17 had small subpleural blebs and developed spontaneous pneumothorax.

LIGHT MICROSCOPY
The morphological lesions observed by light

microscopy in slides from tissues embedded in paraffin were tabulated (Table). At least two slides per case were reviewed by a panel of three pathologists, including one outside consultant. The lesions were identified according to the nomen-

Table *Light microscopy lesions in desquamative interstitial pneumonitis*

	Early (Cases 1–6)	Intermediate (Cases 7–10)	Late (Cases 11–30)
Number of patients	6	4	20
Age (average)	36	53	56
Age range	28–48	39–62	46–67
Males	4	2	10
Females	2	2	10
Intraalveolar cellular clumps	2+[1]	2+	2+
Lymphocytic infiltration			
Alveolar wall	0	1+	2+
Lymphocytic nodules	0	1+	2+
Eosinophils infiltration			
In clumps	2+	2+	2+
In alveolar walls	2+	2+	2+
Pulmonary fibrosis			
In alveolar wall	1+	2+	3+
In interlobular septum	0	2+	2+
Pleural	0	2+	2+
Honeycombing (lung destruction)	0	0	2+
Atypical epithelium lining air spaces	0	0	2+
Mucus in air spaces	0	0	1+
Muscle increase	0	1+	2+
Arteries, medial thickening	0	1+	2+

[1]The values tabulated are obtained by dividing the number of + by the number of subjects in each group.

clature depicted in the table and arbitrarily quantitated as 0 when absent and 1+, 2+, 3+, and 4+. The 1+ positive quantitation represented the presence of at least one lesion per slide. Since the size of the microscopic section varied from case to case, a uniform criterion was used to define the diagnosis of DIP which was established when two lobules of Miller had a minimum of two cellular clumps in the intraalveolar air spaces. Clumps were defined as cellular aggregates containing 50 or more cells. The six cases examined, presumably at an early stage (patients 1 to 6 in the table), presented conspicuous filling of alveolar spaces by clumps of aggregated cells. This lesion was distinctive for DIP (Figure 1) but was patchy in our slides while others had described uniformity and extensive involvement (Liebow *et al.*, 1965; Gaensler *et al.*, 1966; Howatt *et al.*, 1973). Four of the six cases presented minimal lymphocyte infiltration of the alveolar walls, mostly in discrete groups of well-differentiated cells with no germinal centres. One of the patients had minimal hyperplasia of the lining cells with foci of prominent cuboidal cells.

The alveolar walls presented discrete changes, mostly oedema in one case, and some focal thickening in two others. The bronchioles had adjacent tissue inflammation and also clumps of cells in the lumina. The alveolar walls and cellular clumps had prominent eosinophils lined in rows or forming small groups. Intermediate and late stage cases were defined because the intermediate ones, patients 7, 8, 9, and 10, had focal areas of air spaces filled with DIP clumps and evidence of alveolar wall fibrosis while the late stage lesions were characterised by honeycombing, secretion accumulation, and metaplastic epithelial lining of the cystic spaces (Table, cases 11 to 30).

The characteristic presence of clumps occurred in all forms of the disease, the predominant cells appearing to be alveolar macrophages. Variations were observed in the intraalveolar clumps; the early cases had occasional neutrophils while the late stages showed more compact aggregation of cells and occasional attachment to the alveolar wall. The cells forming the clumps were on average 20 μ in diameter. Giant cells 40 to 60 μ in diameter were found intermingled with eosinophils and lymphocytes (Fig. 2). Iron staining demonstrated that the cells forming the clumps had iron deposits in cytoplasmic organelles in approximately 50% of the cases. The slides from the 20 cases estimated to be late stages of the disease showed prominent fibrosis with abundant ground substances replacing the structure of the thickened alveolar walls. These cases also presented marked lung fibrosis with cyst formation and loss of alveolar walls which for descriptive purposes was accepted to be honeycombing. The cysts were lined by granular pneumocytes and with bronchiolar epithelial cells and frequently contained abundant mucous material.

High-resolution light microscopy This material was embedded in resin. The clumps observed in the terminal air spaces had predominant large ovoidal cells with cytoplasmic granules. Their nuclei were vesicular and had only rims of toluidine blue stained chromatin and a small single nucleolus. Because of fixation and processing they were slightly larger than in the slides from the paraffin-embedded material. Eosinophils were observed in the early and late stages in the clumps and in the interstitium. Most of the early cases showed prominent granular pneumocytes in the littoral population but hyperplasia was absent or minimal. Few ciliated cells were observed in the air spaces. Mast cells were prominent in the interstitium in both early and chronic stages. The cellularity of the intraalveolar clumps was more
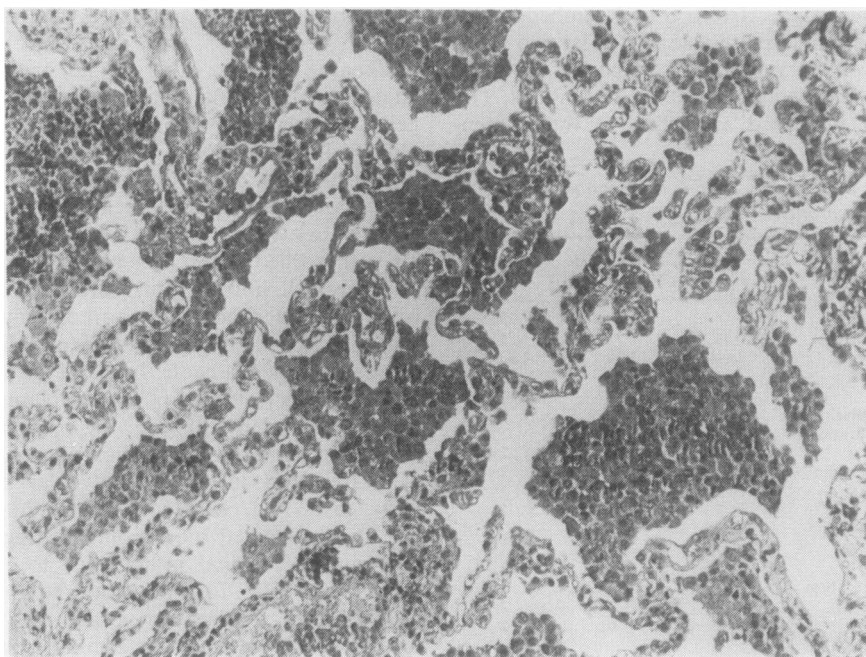
Fig. 1   *Case 3 (33-year-old man). Shows an early stage of DIP since there are minimal alveolar wall lesions. The intraalveolar clumps are focal (Haematoxylin and eosin ×68).*

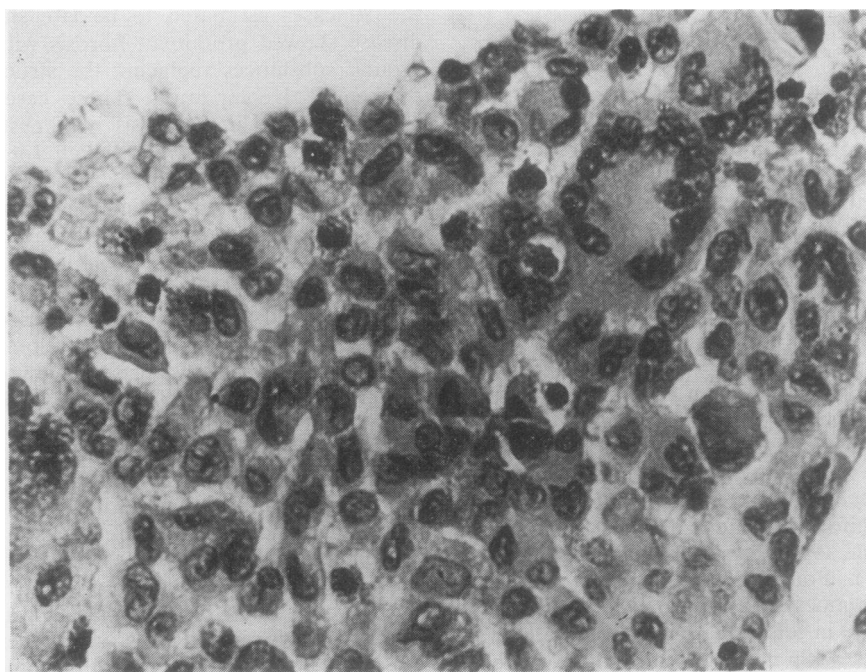Fig. 2   *Case 21. This characteristic intraalveolar clump is formed by epithelioid cells. giant cells, and eosinophils (H and E ×375).*

distinct in the 1 μ thick sections which showed a prominent variation in cellular size and the occasional presence of multinucleated giant cells. Slides from the early stages of the disease showed that the periphery of the clumps had more loose cells while more intercellular contact was observed between the elements present in the core of the clump. The cells lining small fibrosed terminal air spaces had lamellar bodies and organelles characteristic of type II cells, the granular pneumocytes. Bronchiolar epithelium was also found lining the revised air spaces.

Imprints Small pieces of lung biopsies, approximately 0·2 cm in diameter, were used for making cellular imprints on glass slides. The imprints were fixed in ethanol-ether. Unfixed frozen lung material was also used to make cellular imprints. The early stage cases provided abundant cells which were easily visualised by the phase microscope, regular light microscopy, and after cytological staining. The cells were aggregated in sheets of 200 or more but smaller groups or single cells were also seen (Fig. 3). The predominant cells showed abundant blue cytoplasm (Wright's staining). With haematoxylin and eosin the cyto-plasm stained pink, and giant cells with two or more nuclei were prominent. The cytoplasm stained positive with pyronin, resulting in a metachromatic pink colour. Imprints from the late stages of the disease presented sheets formed by a smaller number of cells (average 30–40 cells). The nuclei were vesicular and paracentral, usually with a prominent nucleolus and a rim of stainable chromatin. The cytoplasm contained PAS positive granules, and in approximately one-half of the cases there was material which stained positive for iron. Measurements of these enlarged alveolar macrophages in imprints showed that the most abundant cells had diameters of 25 μ, which is a measurement 10 to 20% greater than in the paraffin-embedded tissue. The giant multinucleated macrophages had diameters of 50, 60, and 80 μ. Imprints from early and late stages had from 3 to 5% eosinophils.

Electron microscopy The ultrastructure examination of this study was performed in biopsies obtained from four cases which were classified to be in an early stage by light microscopy because of the minimal or absent alveolar wall fibrosis. Additional electron microscopy was done in 14
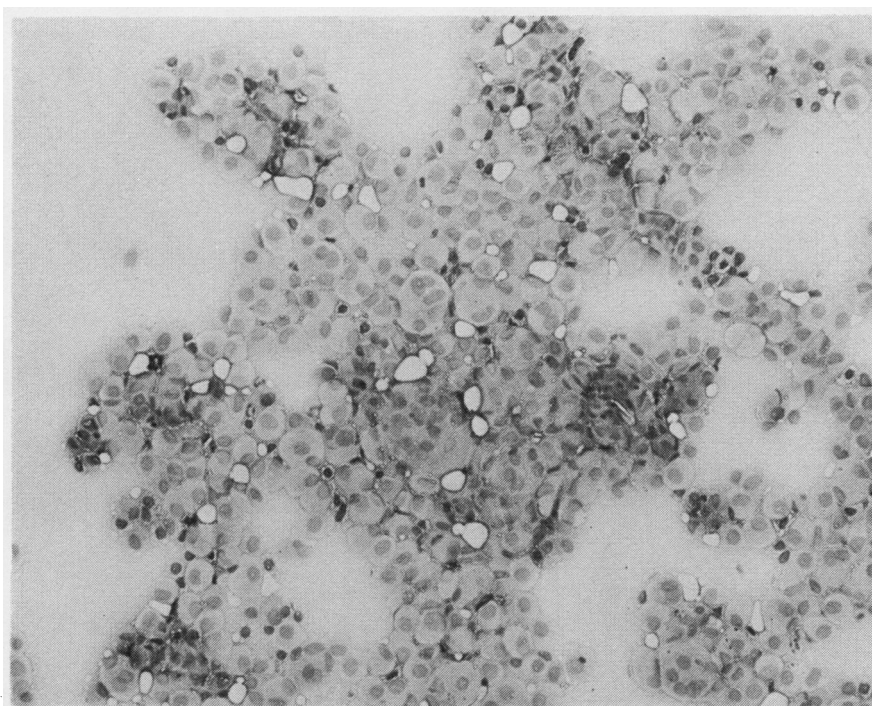

Fig. 3 *Case 6. Lung cellular imprint which presents sheets of cells, presumably identical with the intraalveolar clumps. There are abundant epithelioid cells, giant cells, and eosinophils (H and E ×137).*

cases which had honeycombing and extensive fibrosis. Each case had 50 resin blocks containing small and large lung samples from which six specimens were cut at 1 μ thickness and examined by light microscopy to obtain areas which had alveolar structures or spaces containing cellular clumps. The early lesions were searched to obtain sections of the alveolar wall and to visualise the different cells found in the intraalveolar clumps. Early lesions observed in DIP were studied in three cases which clearly showed that the clumps in the air spaces had a heterogenous population with alveolar macrophages, eosinophils (Fig. 3), lymphocytes, and occasional tangential sections of granular pneumocytes. The most abundant alveolar macrophages had diameters of 20 to 30 μ but larger elements and giant cells were also present. The smaller alveolar macrophages had the ultrastructure of young or immature monocytes with no visible lysosomes, few mitochondria,

and few cytoplasmic membranes (Fig. 4). Some cells presented abundant lysosomes, their cytoplasm staining positive with the methyl green pyronine method, suggesting active protein synthesis, but their rough and smooth endoplasmic reticulum cisternae were poorly developed. Frequently their cytoplasmic inclusions had darker, smaller granules and conglomerates of electron dense material which contained iron positive material when stained histochemically (Figs 5 and 6). These cells had the ultrastructure described for epithelioid cells by Adams (1974). Screening of the DIP aggregates from the early and late cases showed that in some areas the macrophages were adjacent and had an interdigitating process while in the periphery of the clump the cells were free. Examination of the compact cellular aggregate showed that interdigitation was not accompanied by the formation of intercellular complexes. The cytoplasmic
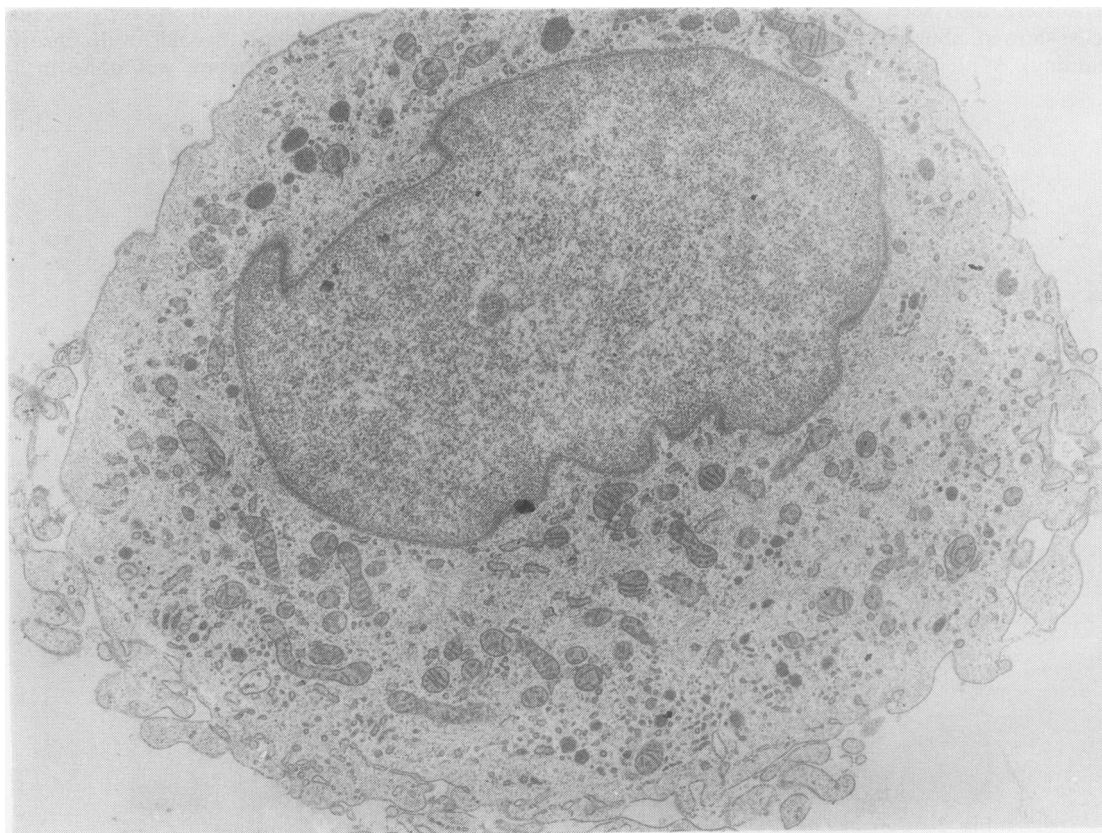

Fig. 4   Case 6. Electron micrograph presents a free alveolar macrophage with average cell diameter of 12μ. This macrophage has few lysosomes. Tissue has been fixed in Millonig's fluid (×11 200).
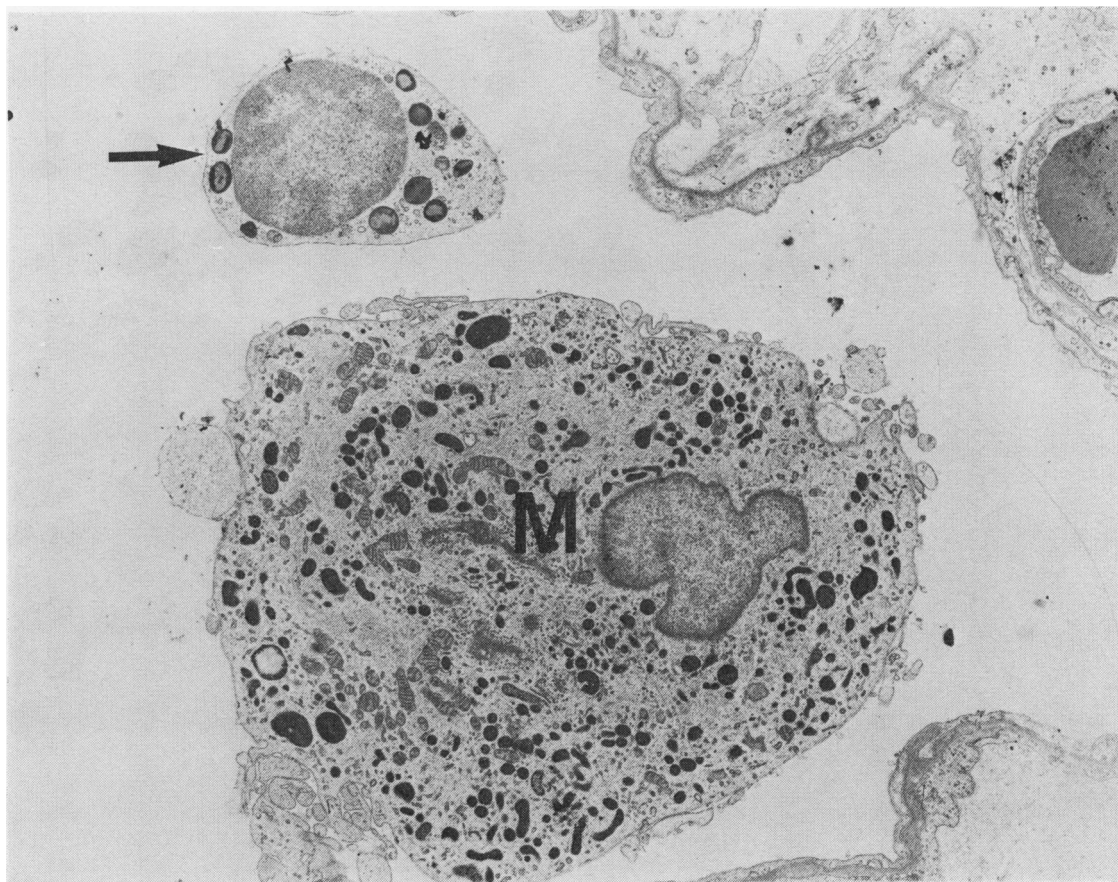
Fig. 5 *Case 6. Electron micrograph shows an alveolar macrophage (M) and an eosinophil (arrow) present in an alveolar space. This enlarged macrophage contains abundant dark-stained lysosomes in the cytoplasm and it has an average diameter of 18 μ (Millonig ×5160).*

organelles of the alveolar macrophages were abundant but variable, the multinucleated giant phagocytes had numerous and prominent lysosomes which occasionally had darker material and may represent iron containing granules. Numerous alveolar macrophages had prominent cytoplasmic bundles of filaments (Fig. 7).

Atypical cases Atypical cases were defined as such because they had morphological variations from the defining features outlined in the table. Four cases were considered atypical forms of DIP. One of the variations was seen in cases 15 and 24. The variations consisted in the presence of epithelial giant cells with giant deformed nuclei containing eosinophilic inclusions. At higher resolution and by electron microscopy these cells had the organelles characteristic of enlarged granular pneumocytes, namely epithelial micro-

villi on the alveolar surface and lamellar bodies in the cytoplasm. These giant granular pneumocytes were always adherent to basement membrane material. The eosinophilic nuclear inclusions were observed to be cytoplasmic infolds surrounded by irregular nuclear membranes and interpreted to be outside the nucleus. Cases 1 and 2 were classified to be at the early stage since the lung had no alveolar wall lesions. The imprints and tissue examination failed to demonstrate the presence of eosinophils which were observed in all other specimens.

Necropsies None of the patients forming this series had a second lung biopsy but six died and necropsy material was obtained in three. Patient 15 of Liebow's (1965) series, also number 15 in this group, died eight days after biopsy. Formalin fixed tissue was embedded in resin and studied by
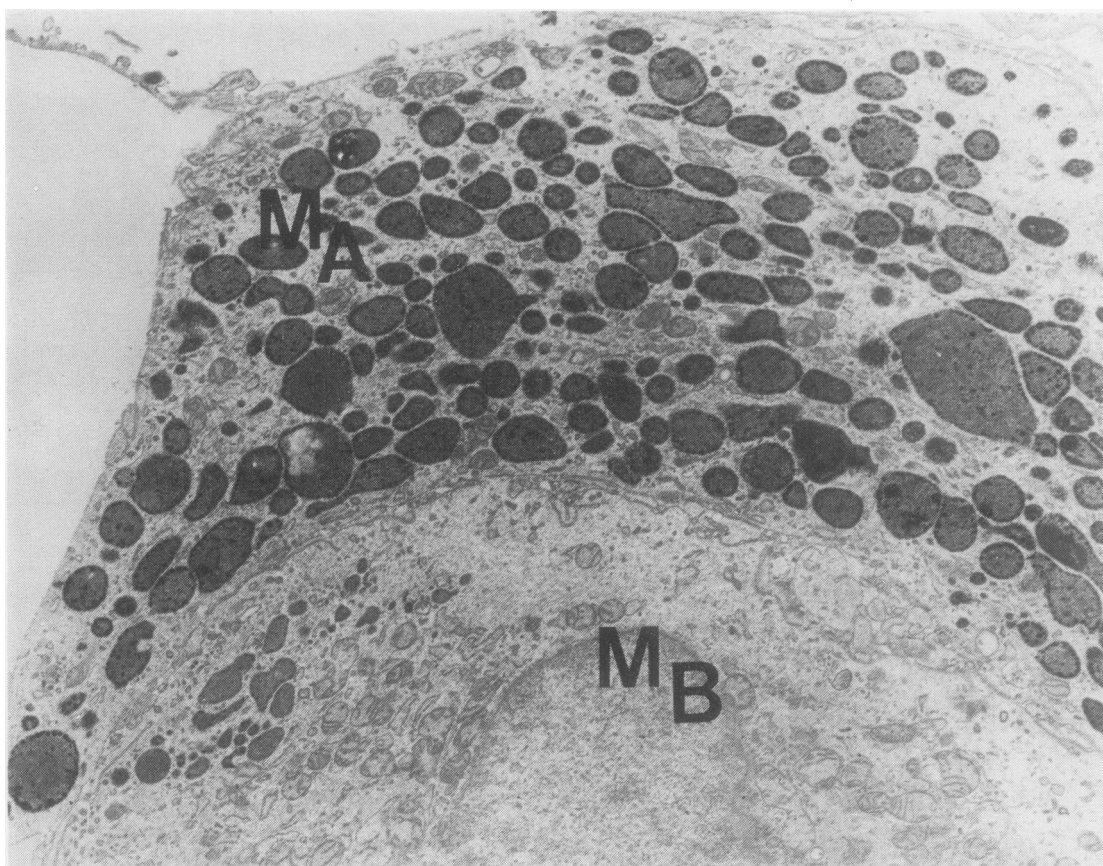
Fig. 6   Case 6. Electron micrograph depicts two adjacent, aggregated alveolar macrophages (M_A and M_B). Cell M_A has abundant lysosomes with dark small granules, probably containing iron. The cells have interdigitating prolongations (Millonig $\times 31\,000$).

light and electron microscopy. This 51-year-old patient's biopsy material had giant cells in the alveolar spaces which had microvilli, lamellar bodies, and the ultrastructure of type II granular pneumocytes. The biopsy material also showed alveolar macrophages and eosinophils in the clumps. Sections from all lobes were examined and revealed extensive interstitial fibrosis, foci of metaplastic changes of the alveolar lining cells with cylindrical and epidermoid epithelium, and occasional accumulation of mucus. Hyaline membranes and fluid were prominent exudative lesions. Purulent bronchopneumonia contributed to the patient's death. Few intraalveolar cell clumps were found focally in the sections.

Necropsy permission for case 29 authorised only examination of the lung biopsy site three weeks after the operation. Microscopic slides showed fibrinous exudate, honeycombing, cellular interstitial inflammation, and purulent bronchopneumonia. There was no evidence of the typical intraalveolar clumps. Necropsy of case 18 was performed four years after lung biopsy and also showed extensive lung fibrosis, honeycombing, and prominent epithelial metaplasia of the pulmonary cystic lesions and terminal air spaces. The postmortem examination showed no evidence of the characteristic intraalveolar aggregation of cells.

Discussion

The histological identification of DIP is outlined by Liebow et al. (1965) and Gaensler et al. (1966) but the pathogenesis, incidence, radiology, course, aetiology, and differential diagnosis are still con-
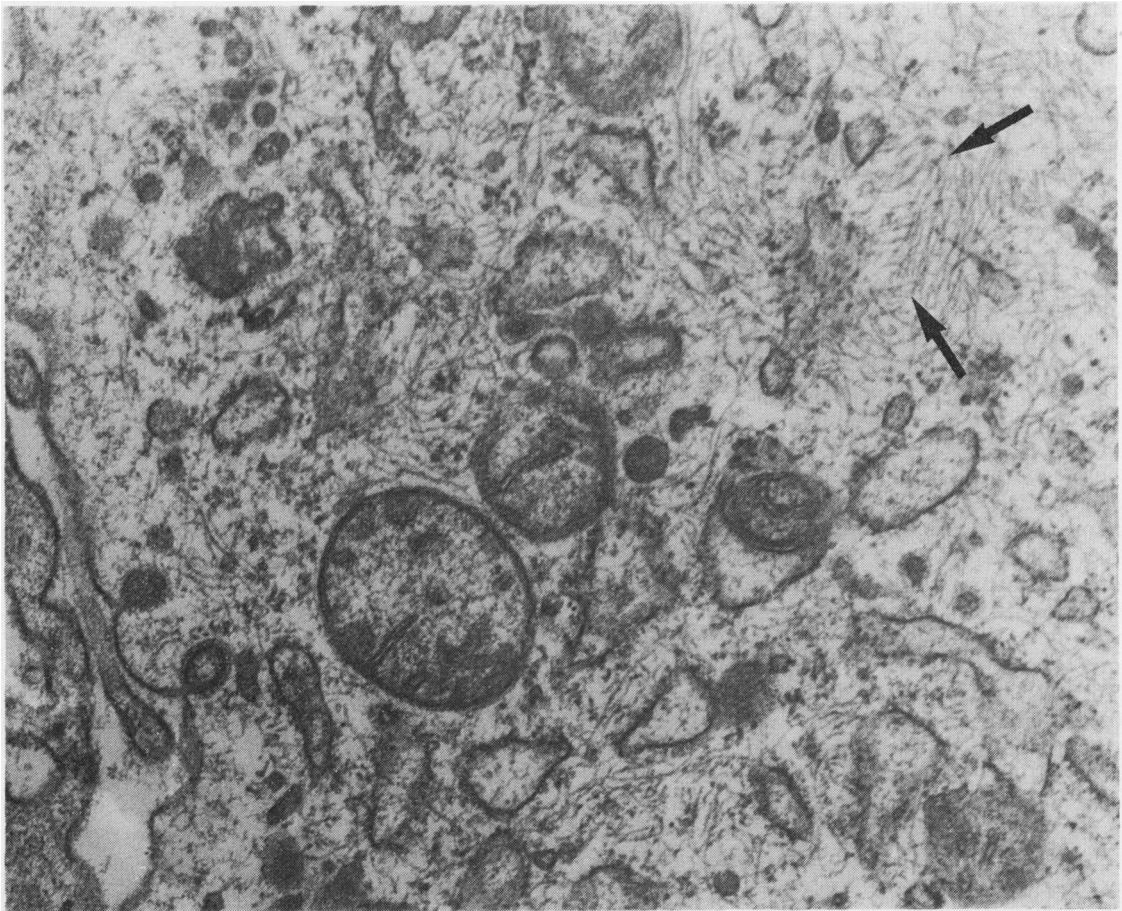
Fig. 7   *Case 6. Electron micrograph shows the cytoplasm of one alveolar macrophage belonging to an intraalveolar clump which contains abundant microfilaments (arrows) (Millonig ✕56 000).*

troversial or unknown because of insufficient information, various deviant features, alternative interpretations of the available data, and the difficulties encountered when attempting to separate DIP from other forms of chronic interstitial pneumonitis (Scadding and Hinson, 1967; Scadding, 1970; Andersen and Fontana, 1972; Lemire *et al.*, 1972; Howatt *et al.*, 1973; Adams, 1974; Kinjo *et al.*, 1974; Carrington *et al.*, 1976).

Liebow *et al.* (1965) include 18 biopsies and one necropsy which present the following morphological features: (1) group of cells in the alveolar spaces, presumably of epithelial origin; (2) absence of necrosis, hyaline membranes, and fibrin; (3) minimal or absent mural fibrosis; (4) monotonous uniformity; and (5) lymphocyte infiltration. Both Liebow *et al.* (1965) and Gaensler *et al.* (1966) believe that DIP is a

different disease entity from the usual type of interstitial pneumonitis (UIP) since DIP has the microscopic desquamative pattern, presumably a more benign course, and it appears to have a better response to corticosteroid administration.

Several reports have confirmed the morphological observations but the clinical presentation, radiology, and progression showed marked variations, extending from asymptomatic patients (Kinjo *et al.*, 1974) to a short and fatal course (Howatt *et al.*, 1973). Progression to mural fibrosis, honeycombing, and loss of pulmonary parenchyma has been described in the series published by Lemire *et al.* (1972), Gaensler *et al.* (1966), Scadding and Hinson (1967), Scadding (1970), and Patchefsky *et al.* (1971, 1973a, b). Carrington *et al.* (1976), in a recent publication, summarise their criteria which separate DIP and

UIP into two different morphological pulmonary lesions but they believe that DIP and UIP may present similar radiological and clinical patterns, produce equal physiological abnormalities, and that both may progress to honeycombing and fibrosis.

Lemire *et al.* (1972) report eight patients whose lungs show desquamative patterns similar to Liebow's outline of DIP in two instances while three patients had lesions considered intermediate because of fibrosis and desquamative patterns and three other cases presented only diffuse fibrosis. Scadding and Hinson (1967) and Scadding (1970) present a similar series and suggest that DIP and UIP are morphological variations of chronic interstitial pneumonitis which may be present or absent at any stage of the disease but favour the desquamative pattern as an early stage. Scadding and Hinson (1967) suggest the name diffuse fibrosing alveolitis to include what they consider to be morphological variations of one pulmonary disease. They report cases presenting intraalveolar mononuclear cell exudate, cases with desquamative and alveolar wall fibrosis, and others in which only diffuse fibrosis is observed. There is histological evidence of the persistence of the desquamative pattern several years after the original diagnosis (Gaensler *et al.*, 1966; Goff *et al.*, 1967; Bates *et al.*, 1971) while in other cases the intraalveolar clumps have decreased in number (Scadding and Hinson, 1967) or are not found in sequential biopsy or necropsy material as observed by Patchefsky *et al.* (1973a) and in this series.

This study is based on the histopathological diagnosis and the tabulation of the morphological changes observed in 30 lung biopsies. The localisation of tissue components in resin-embedded lung specimens allows the ultrastructural identification of cell populations which show that the intraalveolar desquamative patterns are formed by accumulation and aggregation of alveolar macrophages intermixed with lymphocytes, giant cells, and eosinophils. It is assumed that previous reports of type II cell desquamation may be explained because of osmiophilic concentric whorls present in formalin fixed alveolar macrophages, tangential sectioning of the alveolar wall, granular pneumocyte lining of adherent clumps, metaplastic increase of granular pneumocytes, lung atelectasis, reduction of size of air spaces, and frequent postoperative collapse of the lung tissue. Our observations suggest that the accumulation and aggregation of alveolar macrophages must be considered the primary phenomenon of DIP while

the increase in number of granular pneumocytes and the alveolar wall fibrosis may be secondary events (see Table).

The mechanism of alveolar macrophage clumping offers many interesting alternative explanations which may depend on the biological properties of the host, alveolar cells, or structures of the pulmonary parenchyma. Damaged and dead cells agglutinate rapidly but lack of morphological evidence of cell death in the clumps fails to support this simple mechanism. The surface of most cells is known to have anionic charges which are mainly provided by sialic acid molecules oriented on the outer surface of the plasma membrane. A nonspecific neutralisation of these negative charges may occur when proteins or other charged molecules accumulate in the alveolar fluids. Metaplastic changes in the lining of the revised terminal spaces with accumulation of plasma and mucous material may contribute to the persistence of the lesions. Lastly, the alveolar macrophage clumping may depend on a cell mediated hypersensitivity stage which could require T lymphocytes and the production of lymphokines to induce macrophage immobilisation. One attractive hypothesis is to explain the cellular inflammatory infiltration, alveolar wall fibrosis, and destruction to be secondary to products derived from the immobilised alveolar macrophages. This speculative view is similar to the hypothesis of Heppleston and Styles (1967) and Kilroe-Smith *et al.* (1973) for the pulmonary lesions observed in silica pneumoconiosis which proposes that silica pneumoconiosis or the alveolar macrophage exposure to silica *in vitro* induces the release of fibrogenic factors.

The entity described by Liebow *et al.* (1965) and Gaensler *et al.* (1966) has characteristic but not specific features which, to our surprise, are not frequently observed in our series. The clinical onset and symptoms are well described in the literature. Our patients follow a similar pattern but DIP is not found to be the initial or preoperative diagnosis in any of the 30 records. The apparent explanation is probably that the cases studied by the original group (Liebow *et al.*, 1965) were observed at a relatively early stage of the disease when an alveolar pattern is frequently found in chest radiographs. The most difficult morphological diagnosis encountered is when attempting to differentiate idiopathic chronic eosinophilic pneumonia from early and intermediate stages of DIP since both lesions present macrophage clumping in the alveolar spaces and eosinophilic infiltrates. The presence of fibrin in eosinophilic

pneumonia is not a distinctive feature since it may represent an acute phase of a cellular inflammatory exudate; furthermore, fibrin has been shown to be present in the alveolar lesions of our cases of DIP studied with immunofluorescence techniques. The vasculitis described in idiopathic chronic eosinophilic pneumonia (Liebow and Carrington, 1969) is not a frequent or specific mural lesion and it may again be a secondary feature present at an early stage. Both entities, DIP and idiopathic chronic eosinophilic pneumonia, are suspected to be hypersensitivity pneumonitis and develop in individuals in which an immunological mechanism may be responsible for the inflammatory reaction (Leroy, 1969). Despite the presence of clinical, radiological, and morphological differences which exist between DIP, UIP, Hamman Rich syndrome, diffuse fibrosing alveolitis, and chronic idiopathic eosinophilic pneumonias, the similarity of the pulmonary morphology and the occurrence of cases with mixed features support the view that all may have common variations dependent on a presumed similar pathogenesis or the stage of the disease.

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