

The average pulmonary blood volume in normal persons was 211 ml./m.<sup>2</sup>, in patients with mitral regurgitation 266 ml./m.<sup>2</sup>, and in those with mitral stenosis 419 ml./m.<sup>2</sup>

In patients with mitral stenosis the pulmonary blood volume could be related to pulmonary symptoms like exertional dyspnoea, haemoptysis, and paroxysmal nocturnal dyspnoea. Pulmonary blood volume could also be related directly to left atrial and pulmonary arterial pressures and inversely to pulmonary vascular resistance.

It is suggested that estimation of pulmonary blood volume may be an additional useful parameter to explain pulmonary symptoms of patients with mitral stenosis.

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## Erythema Nodosum and Psittacosis: Report of Five Cases

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The list of aetiological agents alleged to provoke erythema nodosum is a long one, and the frequency with which different factors have been recorded varies with country, climate, age distribution of the examined community, and the collectors' particular interest. In the relatively unselected series reported by Vesey and Wilkinson (1959) 25 (36%) of 70 cases had a proved or presumed streptococcal infection, 25 (36%) had either bilateral hilar lymphadenopathy or sarcoidosis, and only four cases had tuberculosis. In Great Britain, once streptococcal sensitization, sarcoidosis, and tuberculosis have been excluded, an aetiological diagnosis is not often made, although an unusual provoking agent may be discovered under epidemic conditions. Erythema nodosum occurring in coccidiomycosis was first described in this way (Dickson, 1937).

We report here five cases of typical erythema nodosum which occurred in patients believed to be suffering from psittacosis acquired during an epidemic of this disease in East Anglia (Barrett and Greenberg, 1964). In every case the rash was erythematous, nodose, multiple, tender, symmetrical, and confined to the extensor surfaces of the limbs, and it faded through a spectrum of colours like that of a bruise.

### Case 1

A woman aged 44 was admitted to hospital on 14 June 1964 with a history of rash on the arms and legs and a productive cough coming on a few days after a sore throat. There was no known contact with birds and she had not taken medicine of any sort prior to the onset of the rash. On examination she had extensive and typical erythema nodosum on the legs and a rash resembling erythema multiforme on the arms. There were no other abnormal physical signs.

Investigations showed: haemoglobin 11.1 g./100 ml.; W.B.C. 7,500/c.mm.; E.S.R. 95 mm. in the first hour (Westergren). Sputum microscopy showed pus cells, but only commensal organisms were isolated on culture. No acid-fast bacilli were seen or cultured, and the Mantoux reaction to 1/10,000 and 1/1,000 was negative.

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Chest x-ray examination on admission showed nothing abnormal. A complement-fixation test for psittacosis on 18 June (two and a half weeks after onset of the illness) was positive at a titre of 1/512. Complement-fixation tests for Q fever, adenovirus, and Eaton agent were all negative at less than 1/8. Antistreptolysin titre on 23 June was 330 Todd units/ml. Biopsy of a nodose lesion showed changes typical of erythema nodosum (Dr. J. Rack).

The patient subsequently developed a transient arthralgia with pyrexia, and an area of coarse crepitations at the left lung base. This rapidly settled on symptomatic treatment only, and she was discharged two weeks later, her erythema nodosum having faded very considerably. At a follow-up examination the chest x-ray picture was normal, E.S.R. was 14 mm./hr., Mantoux to 1/100 was negative, and the psittacosis titre had fallen to 1/64.

### Case 2

A woman aged 43 was admitted with a five-day history of general malaise followed by a rash on the arms and legs and a productive cough. She had taken four tablets of Drinamyl (amylobarbitone with dexamphetamine) for malaise about 48 hours prior to development of the rash. She was admitted on 5 June 1964 and found to have severe and typical erythema nodosum on the extensor surfaces of the arms and legs. There were crepitations at the left lung base but no other abnormal physical signs.

Investigations showed: haemoglobin 13 g./100 ml.; W.B.C. 20,000/c.mm. (86% neutrophil polymorphs); E.S.R. 105 mm. in the first hour (Westergren). Sputum contained pus cells, but no pathogens were isolated on culture. Microscopical examination and culture for acid-fast bacilli proved to be negative on three occasions. Only commensal organisms were cultured from a throat swab. Chest x-ray examination showed dense consolidation involving the apical segment of the left lower lobe. Mantoux 1/1,000 was negative. A complement-fixation test for psittacosis on the day prior to admission was 1/32; 12 days later it had risen to 1/256. Complement-fixation tests for influenza A and B, Q fever, adenovirus, and Eaton agent were all less than 1/8 on two occasions. Antistreptolysin titre was 100 Todd units/ml. on two occasions.

Treatment with penicillin and subsequently ampicillin brought improvement, the erythema nodosum fading within 10 days. The chest x-ray picture five weeks later was normal and the complement-fixation titre to psittacosis was 1/512.

**Case 3**

At the end of March 1964 a woman aged 43 developed a sore throat with a productive cough; two weeks later she developed classical erythema nodosum on the shins. Chlortetracycline and later erythromycin were given, and her symptoms slowly subsided. In May, when there were some residual brownish patches on the front of the shins, a chest x-ray film was clear and a Heaf test was negative. In July a repeat chest x-ray film remained clear. She now supplied the information that before the onset of her illness she had been in contact with a known case of psittacosis, although she herself had not had any direct contact with birds. Her complement-fixation test on 13 July gave a positive titre to psittacosis of 1/1024.

**Case 4**

A woman aged 29, 20 weeks pregnant, developed a sore throat during the first week of June 1964. Erythema nodosum appeared 10 days later. There were no respiratory symptoms, and at the time of her illness the E.S.R. was 55 mm. in the first hour (Westergren), W.B.C. 8,000/c.mm., and the antistreptolysin titre 50 Todd units/ml. She was treated with penicillin, and three weeks later, apart from the fading erythema nodosum, there were no abnormal physical signs and the chest x-ray film was clear. Complement-fixation test on 29 June showed a titre of 1/256 to psittacosis.

**Case 5**

A woman aged 54 presented in late August 1964 with typical and extensive erythema nodosum, which had come on five days after a sore throat and a productive cough. The cough persisted for some time but the erythema nodosum faded within three weeks. The psittacosis complement-fixation test on 23 September 1964, some three weeks after the onset of the erythema nodosum, was 1/256. She was treated with a course of demethylchlortetracycline and recovered.

**Discussion**

Although psittacosis is normally an uncommon disease in Great Britain, a minor epidemic occurred in East Anglia during the spring and summer of 1964, a total of 61 cases being found by the Public Health Laboratories, Cambridge, to have complement-fixation titres to psittacosis of 1/32 or higher. This laboratory normally records no more than two or three cases per annum of elevated complement-fixation titres of psittacosis.

In a detailed review of this disease the only skin manifestation mentioned by Sturdee and Scott (1930) was "rose spots," also described by Hutchison *et al.* (1930) and by Horder and Gow (1930) (Horder's spots). This rash resembles that seen in typhoid, and its distribution is not like that of erythema nodosum. Although erythema nodosum is a relatively common disease, it is highly unlikely that five cases would have occurred by chance in patients having high psittacosis titres.

We have found only one case report suggesting an association between erythema nodosum and psittacosis. Brocard *et al.* (1961) reported the case of a 29-year-old woman who had developed bilateral hilar adenopathy with erythema nodosum some two weeks after the resolution of a chest infection. There was a history of exposure to pigeons and radiological evidence of pulmonary consolidation. Psittacosis complement-fixation titres were initially 1/80, but subsequently rose to 1/320 during development of the erythema nodosum. The skin rash faded within 10 days, but the hilar adenopathy was still present after four months. Because the erythema nodosum and hilar adenopathy developed two weeks after the chest illness, and because the course of her subsequent illness resembled that of sarcoidosis rather than psittacosis, it is possible that the relationship of the erythema nodosum to the psittacosis illness was fortuitous.

There are few reports in the literature of erythema nodosum developing in association with a virus disease. Wallgren (1926) records two cases of erythema nodosum occurring in children

with measles, but both had recently had pulmonary tuberculosis. In view of the relationship of the psittacosis virus to that causing lymphogranuloma venereum, the series reported by Hellerström (1929) is of particular interest; 4 of his 47 lymphogranuloma cases had erythema nodosum, and none of these showed radiological evidence of tuberculosis. In three of the four cases erythema nodosum developed subsequent to the Frei intracutaneous test. In no case did the lymphogranuloma illness present with erythema nodosum.

All the cases reported by us were in women, and four out of the five were aged 43 to 54—rather older than is usual for erythema nodosum, most reported cases occurring in the third and fourth decades. In this context it is of interest to note that Vesey and Wilkinson (1959) recorded erythema nodosum in seven "bronchitic" women aged from 48 to 54, the rash following an exacerbation of their chest symptoms. Frankel (1945) reported a severe type of erythema nodosum in 14 women over the age of 30, but does not mention radiological evidence of pulmonary disease.

There is a marked similarity in the history given by our five patients—four of them had a sore throat and all a productive cough prior to the erythema nodosum.

It is noteworthy that tuberculin-testing, though carried out in only three of the five cases of erythema nodosum here reported, was in each case negative. No other evidence of sarcoidosis was obtained, and in no case did hilar adenopathy develop. This raises the question of the significance of a negative tuberculin test in erythema nodosum.

Erythema nodosum occurring in middle age is not very common, and it is suggested that if a case occurs in this age group the question of an unusual provoking agent, such as a virus, be raised.

**Summary**

Five cases are described in each of which typical lesions of erythema nodosum occurred in association with a raised complement-fixation titre to psittacosis. In no case did hilar adenopathy develop. All the patients were women, four of the five being aged over 40, in contrast to the usual age distribution of erythema nodosum. It is suggested that in cases of erythema nodosum occurring in an older age group the question of a viral aetiology be considered.

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ADDENDUM.—A 39-year-old woman was admitted to hospital in April 1965, having fourteen days earlier developed a sore throat and cough, and, two days prior to admission, erythema multiforme and erythema nodosum. The complement fixation test to psittacosis was 1/2,054. Chest x-ray film was negative, antistreptolysin O titre was less than 50 units/ml., and tuberculin reaction was negative to 1/100.

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