

almost 3% have a raised serum creatinine (unpublished observations), in 27 months only 10 from all age groups reached a point where they would usually be regarded as needing RRT (6 who died of renal failure and 4 who started RRT). This is a small fraction of the number that would be expected to progress to end-stage renal failure if the incidence of nephropathy among diabetic patients in Britain approached that in Denmark,¹² where more than 40% of patients diagnosed under 31 years of age had nephropathy and two-thirds of these died of renal failure.¹³ Acceptance rates of diabetic patients for RRT in Nottingham could only have matched those in Scandinavian countries and the USA^{1,14} if elderly or severely disabled patients had been treated, cases in which treatment may be withdrawn in other countries.¹⁵ We suggest that fluid retention may be a better indicator of the need to start RRT than serum creatinine concentration in some older diabetic patients, but whether early treatment would prolong survival needs to be assessed prospectively.

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Environmental Health

RESPIRATORY ALLERGY TO INHALED BAT GUANO

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Summary In the Sudan many asthmatic patients attribute their symptoms to inhalation of bat droppings. Design of the roofs of many Sudanese buildings allows black bats to roost; guano drops through cracks in the ceiling into the rooms below where it can be inhaled and cause allergic respiratory disorders. Seven atopic patients seen at Sennar Hospital with bat-related case-histories were investigated. Six had bronchial asthma and allergic rhinitis and one had asthma alone. Extracts of yellow hairy bat, black bat, and bat droppings were made. All seven patients had a positive skin prick test and specific IgE antibodies (RAST) to bat droppings. Three patients also had a positive RAST to both yellow and black bats and one patient to yellow bat. Droppings are probably the major allergen source in bat-related respiratory allergy.

INTRODUCTION

MANY patients seen at Sennar Hospital in the Sudan with asthma attribute their symptoms to exposure to the bats which cohabit their homes and places of work. Bats roost in large numbers in the space below the corrugated iron sheet roof and above the cardboard ceiling which protects the interior of the building from radiant heat. Bats also roost at the point of entry of air-coolers into buildings when the space between the air-cooler and the wall of the building has not been sealed. Bat guano drops into the rooms below through cracks in the ceilings.

We studied seven patients to determine whether their respiratory symptoms were the consequence of allergy to bat

guano, a previously unreported and, in the Sudan, a potentially widespread and preventable condition.

MATERIALS AND METHODS

Study Group

Seven patients (four men, three women, age range 25-45 years) seen during the course of one week at Sennar Hospital were studied (table 1). All were complaining of nasal and/or lower respiratory symptoms which they related to contact with bats. A complete personal and family history was taken including a history of wheezing, allergy, and rhinitis. Peak expiratory flow rate (PEFR) was measured and skin prick tests done. Atopy was defined as one or more positive skin tests to local environmental allergens. Serum was obtained and stored at -20°C for measurement of total IgE and RAST. Chest radiographs were taken and stools examined for parasites when indicated.

Four of the patients worked at Sennar Hospital. One was a radiographer whose place of work was known to be heavily infested with bats. Two others were nurses whose symptoms developed after starting work at the hospital. The fourth was a nursing instructor whose symptoms developed before he came to work in the hospital; the symptoms subsequently improved but recurred after he joined the hospital nursing school. Of the other three patients, one worked as a fire brigade officer in Sennar Sugar factory; he noticed his symptoms 5 years after he started work in the factory. The two other patients had long histories of asthma, one since childhood. One associated her symptoms with exposure to bats but the other did not, although she recognised exposure to bats both in her home and at work.

TABLE 1—CLINICAL DETAILS

Patient	Symptoms		Symptoms provoked		Stool examination	Chest radiograph
	Asthma	Rhinitis	At work	At home		
○	+	+	+	-	-	Normal
●	+	+	+	-	-	Normal
△	+	+	+	-	-	Normal
▲	+	-	-	+	Not done	Normal
□	+	+	+	+	-	Normal
■	+	+	+	+	Not done	Normal
◇	+	+	+	-	-	Normal

+ = positive; - = negative.

All patients either had asthma before the study started or manifested asthmatic symptoms during the study. All but one also had nasal symptoms. Three had a family history of asthma; one was a smoker. Respiratory symptoms occurred at work in six of the seven patients; the seventh patient, a housewife, had moved house on several occasions to avoid bats and improve her asthma. Two patients whose homes were bat infested associated their symptoms both with their places of work and their homes.

At the initial examination PEFR in the seven patients ranged between 250 l/min and 550 l/min. All had normal chest radiographs. Stools were examined in five cases; no ova or worms were found.

Preparation of Extracts

Whole black bat (identified as *Tadarida [chaerephon] major* by Dr J. E. Hill, British Museum [Natural History], London), yellow bat, and bat droppings were defatted in three changes of ether over 24 h and extracted for 16 h in 10 vol Coca's solution (5 g sodium chloride, 2.75 g sodium bicarbonate, and 5 g phenol made up to 1 l with distilled water). Extracts were filtered through Whatman 113V filter paper followed by Sartorius glass fibre filters (SM 13400), dialysed in 'Visking' tubing (Medicell International, London) against three changes of distilled water during 24 h, and lyophilised.

Skin Prick Testing

Skin prick test solutions of the three bat extracts (1 mg/ml concentration of lyophilised powder) were prepared in 50% Coca's solution and 50% glycerol and passed through a 0.22 µm 'Millex GS' filter (Millipore Corp, Bedford, MA) before use. The diluent and histamine dihydrogen chloride at 1 mg/ml were used as negative and positive control solutions, respectively. Skin prick tests were also done with commercial extracts (Bencard, Brentford, Middlesex) of *D pteronyssinus*, cotton flock, *Alternaria alternata*, and *Cladosporium herbarum*, and with the local environmental antigen *C lewisi* (green nimitti midge).

Measurement of Total IgE Antibody

Total IgE measurements were made on the seven sera with Phadebas IgE 'PRIST' (Pharmacia, Uppsala, Sweden) according to the manufacturer's recommendations.

Radioallergosorbent Test (RAST)

Paper discs (Schleicher and Schuell, Keene, NH, no 589/3) were activated with cyanogen bromide. 3 mg of lyophilised bat droppings or black bat and yellow bat extracts was coupled per 300 mg of activated discs by the method of Axen et al.¹

Assay

50 µl serum per disc was incubated for 16 h at room temperature. After washing, 50 µl ¹²⁵I-labelled anti-IgE (Pharmacia Diagnostics) was added to each tube for a second 16 h incubation. After further washing, the tubes were counted in a gamma counter, and the percentage binding of the isotope was calculated. Cord-blood sera with no demonstrable IgE were used as negative controls. To investigate the possible interference of high total IgE in the assay, a serum sample from a subject not exposed to bats with a total IgE of 6600 kU/l was also assayed in the three RAST assays.

TABLE II—RESULTS OF SKIN PRICK TEST

—			Skin prick test			
Patient	Sex	Age	Bat droppings	Black bat	Yellow bat	Total IgE (kU/l)
○	M	45	+++	++	++	876
●	M	35	+++	+++	+++	2188
△	F	35	++	++	—	546
▲	F	37	+++	+++	—	5771
□	F	30	++	++	—	181
■	M	30	+++	+++	++	4862
◇	M	25	++	++	++	297

— = no wheal; ++ = wheal < 3 mm; +++ = wheal 3–5 mm.

RAST Inhibition

RAST inhibition studies were done by means of a 16 h pre-incubation of a positive serum pool (100 µl) from the study patients with four concentrations of the three lyophilised bat extracts (100 µl). The bat RAST assays were carried out and percentage binding of the ¹²⁵I anti-IgE compared with that of the unabsorbed serum pool.

RESULTS

Clinical details of the study patients and their skin test responses to the bat allergens are shown in table II. Patients are represented by symbols which are also used in fig 1.

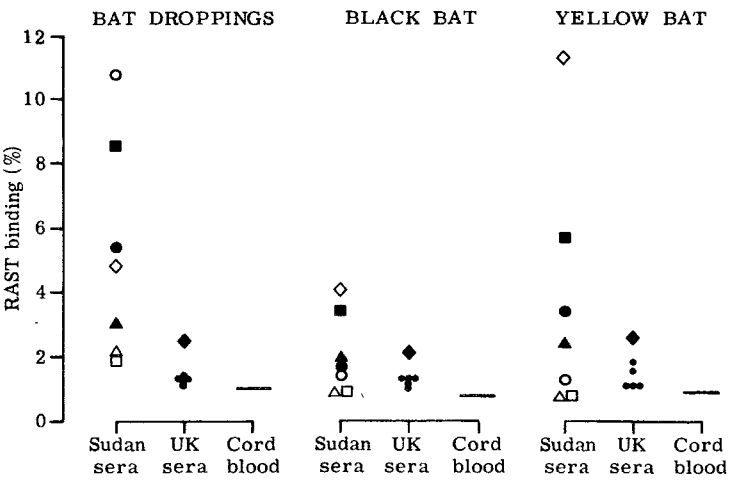


Fig 1—Comparison of RAST ¹²⁵I anti-IgE binding to bat droppings, black bat, and yellow bat in sera from seven Sudanese patients and six UK controls.

Cord blood sera in the same assays indicate the background percentage binding.
◆ total IgE 6600 kU/l.

Skin Tests

All seven patients were atopic, with positive immediate skin prick test responses to one or more of the allergens common in the Sennar area—*D pteronyssinus*, green nimitti midge, or cotton flock.

Extracts of whole black bat and black bat droppings provoked an immediate skin test response in all patients; four patients reacted to whole yellow bat extract. Total serum IgE levels ranged between 181 and 5771 kU/l.

RAST

Fig 1 shows the RAST results, expressed as percentage binding of the isotope. The seven patients all had increased binding of ¹²⁵I anti-IgE isotope in the bat droppings RAST; values ranged from 1.9% to 10.8% (fig 1). Some of the patients also had specific IgE in their sera to black bat extract (isotope binding 0.9–4.1%) and to yellow bat extract (isotope binding 0.8–11.3%). Background levels of the assays tended to be low: cord blood sera gave 1.0% isotope binding in the bat dropping RAST, 0.8% in the black bat RAST, and 0.9% in the yellow bat RAST. Sera from five unexposed UK subjects gave 1.3% mean binding in the assays, while a serum sample (◆) with a total IgE content higher than any in the study (6600 kU/l) gave 2.5% binding in the bat dropping RAST, 2.1% in the black bat RAST, and 2.6% in the yellow bat RAST. The raised specific bat RAST bindings were therefore not attributable to non-specific binding of sera with high total IgE.

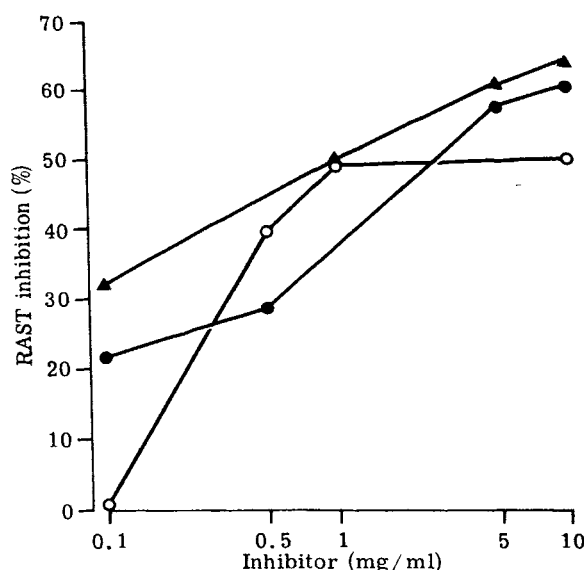


Fig 2—Inhibition of bat RAST assays with serum pool of two bat hypersensitive patients.

- bat droppings RAST inhibited with bat droppings extract.
- black bat RAST inhibited with black bat extract.
- ▲ yellow bat RAST inhibited with yellow bat extract.

RAST Inhibition

Pre-incubation of the patients' positive serum pool with increasing concentrations of the three bat extracts inhibited the RAST assays in a dose-dependent fashion (fig 2), validating the immunological specificity of the assays.

DISCUSSION

Bats are common in the Sudan² and often live in close contact with man. They are recognised as vectors of disease, causing rabies and histoplasmosis. We have found evidence for another bat-related health hazard—IgE mediated allergy to bat droppings, causing asthma and rhinitis.

Our seven patients had asthma and all but one also had rhinitis. Extracts of bats, in particular black bat droppings, provoked immediate skin prick test responses and bound specific IgE in their sera. Guano is probably the main source of allergen. The increased frequency of specific IgE and skin prick test responses to extracts of black bats and their droppings by comparison with yellow bats probably reflects the greater exposure to black bats which congregate in large numbers inside buildings. In contrast, yellow bats roost outdoors in trees with little subsequent human exposure to their guano. The skin test and RAST response to yellow bat extract in our patients are probably due to cross-reactivity with black bat antigens.

Allergy to inhaled bat guano is unlikely to be confined to Sennar; patients from as far as Khartoum (300 km north) and Juba (1200 km south) have attributed their asthma to bats. Neighbouring African countries where building design is similar may also be affected, since many of the sixty-two species of bat found in the Sudan are shared with its neighbours.² Bats also live in the roofs of houses outside Africa.³ In Europe they are known to roost in the roofs of cathedrals, belfries, and galleries, in underground tunnels, and in nesting boxes intended for birds.⁴

In the Sudan attempts have been made to prevent bats roosting in houses and factories. Some of the sugar factories employ special groups to fumigate the roofs of factories and houses, but success is short-lived and bats recolonise their

old living quarters within a few months. Fumigation is one of the means used to "decolonise" ships in British ports.³ Other means tried in the Sudan and elsewhere include the use of light to prevent bats roosting and the stripping of ceilings below the roofs.³ Neither method has proved successful because the bats find enough space and darkness between the wood logs used to support the roof. Chemical repellents placed at bats' entry sites have been successful, but it seems easier and more effective to seal off entry sites once these have been identified.³

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Radiotherapy

EUROPEAN ACCELERATOR FOR RADIOTHERAPY WITH CHARGED IONS

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DESPITE improvements in surgery and chemotherapy, radiotherapy remains one of the most frequently used methods for treating cancer; more than half the patients who get cancer receive radiotherapy at some stage. Advances in radiotherapeutic technique are therefore welcome. The greatest single advance in the past forty years has been the introduction of megavoltage X rays to replace X rays generated at 200-300 kV. The maximum dose from megavoltage beams occurs beneath the skin, sparing the patient the severe skin reactions that were inevitable with conventional X rays. The increased penetration of the beam enables tumours at almost any anatomical location to be treated to a full therapeutic dose while reduced scatter limits irradiation of healthy tissue away from the tumour. Lower absorption of energy in bone has reduced the incidence of radiation-induced fractures. However, little further improvement can be expected, since the optimum energy of an X-ray generator—about 4-15 MeV—is well within the range of modern equipment.¹

Because results with X-ray therapy leave much to be desired, thoughts have turned to other forms of radiation. The first to be tried was fast neutrons, which were used in California as long ago as 1938.² Until lately, fast neutron beams were more comparable with X rays generated at 250 kV than at megavoltage energies. Modern neutron generators, however, based on cyclotrons operating at 40-70 MeV, produce beams whose physical characteristics are similar to those of 4-10 MV X rays.³ The biological effects of fast neutrons are considerably different from those of X rays because ionisation in tissue occurs along the tracks of secondary recoil protons and other ions rather than secondary electrons, giving a greater density of ionisation. Biological experiments have suggested that an increased