normal homozygotes within the range of 61–90 units. Seventeen people with a pseudo-cholinesterase level below 36 units were selected as the *propositi* of family studies. All of them had come to attention because of suxamethonium apnoea unassociated with a disease which might cause a low pseudo-cholinesterase level. These results can now be further extended by taking into account the present family and eight others examined since, making a total of 26 (Table I).

TABLE I.—*Relatives of Patients Presenting with Suxamethonium Apnoea Unassociated with Diseases Causing a Low Pseudo-cholinesterase Level*

People with Plasma Pseudo-cholinesterase <36 Units	Relatives		Plasma Pseudocholinesterase (Warburg Units)			
	Group	No.	<36	36–60	61–90	>90
26	Parents and children	52	3	22	27	0
17	Siblings	31	11	6	11	3
10	Spouses	10	0	0	5	5

If it is presumed that the *propositi* are homozygous, their first-degree relations—parents and children—should be heterozygotes. It is clear from Table I that none of 52 first-degree relatives of the 23 *propositi* had a pseudo-cholinesterase level above 90 units. Thus it can be considered fairly safe to rule out the heterozygous state for the abnormal gene when a level above 90 units is found. On the other hand, more than half of the 52 first-degree relations assumed to be heterozygotes showed a pseudo-cholinesterase level within the lower range of normality—from 61 to 90 units. Thus, within this range an overlap occurs between normal homozygotes and heterozygous carriers. The present family tree shows this particularly well. The enzyme levels of both parents of the *propositus* are found within this “normal” range—61 to 90 units. Yet each of these two, in turn, has one parent with a clearly abnormally low level of 50 and 44 units, respectively. Together they have a child with an enzyme level of 24 units.

There is, obviously, also an overlap at the lower range of the enzyme levels, and values below 36 units seem to include both abnormal homozygotes and heterozygous carriers. Three individuals in the parents-and-children group (Table I) showed values of less than 36 units (26, 28, and 35 units, respectively), and two of these were children of a *propositus* and a spouse with a pseudo-cholinesterase level above 0 units. Thus, in at least two of these it seems possible to rule out the homozygous state. Not enough data have yet been accumulated, but it may well be that the values below 36 units will have to be subdivided into those below 26 units, designating definite abnormal homozygotes, and those from 26 to 35 units, designating both abnormal homozygotes and heterozygotes. Kalow and Staron (1957) have demonstrated that an abnormal enzyme can be the cause of idiopathic familial low pseudo-cholinesterase level. Investigations are in progress, in collaboration with Dr. H. Harris and Dr. Mary

TABLE II.—*Abnormal Gene Causing Low Pseudo-cholinesterase Level*

Pseudo-cholinesterase	Abnormal Homozygotes	Heterozygotes	Normal Homozygotes
<26 units	+		
26–35 “	+	+	
36–60 “		+	
61–90 “		+	
>90 “			+

Whittaker, London Hospital Medical College, to examine the correlation between the findings of the Canadian workers and those of this country. Possibly these studies will throw light on the subdivision of phenotypes proposed in Table II.

Summary

Suxamethonium apnoea is described in a child aged 15 months. This is believed to be the first such recorded observation in an infant. The family has been studied in detail. There was a deficiency of pseudo-cholinesterase in one paternal and in one maternal grandparent, yet only low normal values for pseudo-cholinesterase were found in both parents. The overlap of enzyme levels found for presumed heterozygotes for the abnormal pseudo-cholinesterase gene and for normal individuals is discussed.

We are grateful to Mr. G. H. Macnab, under whose care the patient was admitted into the Hospital for Sick Children, Great Ormond Street, London, and to Dr. R. W. Cope for their permission to use the case notes of this patient.

REFERENCES

- Allott, E. N., and Thompson, J. C. (1956). *Lancet*, 2, 517.
 Anscombe, A. R. (1957). *Pulmonary Complications of Abdominal Surgery*, p. 55. Lloyd-Luke, London.
 Bourne, J. G., Collier, H. O. J., and Somers, G. F. (1952). *Lancet*, 1, 1225.
 Evans, F. T., Gray, P. W. S., Lehmann, H., and Silk, E. (1952). *Ibid.*, 1, 1229.
 ——— (1953). *Brit. med. J.*, 1, 136.
 Harmel, M. H., King, B. D., and Kao, F. F. (1958). *J. Pharmacol. exp. Ther.*, 124, 333.
 Kalow, W., and Staron, N. (1957). *Canad. J. Biochem.*, 35, 1305.
 Lehmann, H., Patston, V., and Ryan, E. (1958). *J. clin. Path.*, 11, 554.
 ——— and Ryan, E. (1956a). *Lancet*, 2, 124.
 ——— (1956b). *Ibid.*, 2, 681.
 McArdle, B. (1940). *Quart. J. Med.*, 9, 107.

EOSINOPHILIA IN CHILDREN WITH ASTHMA AND BRONCHIECTASIS

BY

L. B. STRANG,* M.B., M.R.C.P.

From the Department of Child Health, King's College, University of Durham, at Newcastle upon Tyne

It is well known that asthmatic attacks are often associated with an eosinophilia in the circulating blood and that the bronchial secretions also may contain an excess of eosinophils (Stickney and Heck, 1944; Urbach and Gottlieb, 1946). Blood eosinophilia is regarded as typical of allergic reactions in general, and can be produced experimentally by injections of protein material (Biggart, 1932) or histamine (Vaughn, 1953). It is suggested that the eosinophils are concerned in the transport of histamine which is produced in allergic reactions (Code, 1952; Vaughn, 1953).

The present paper provides evidence that eosinophilia in asthmatic children is not confined to the times of the asthmatic attacks and in general is unrelated to the degree of ventilatory impairment. In addition, eosinophil counts on a group of children with asthma and a group with bronchiectasis are compared in order to evaluate their usefulness in differentiating these conditions.

Methods

Eosinophil counts were performed on 83 children (40 with bronchiectasis and 43 with asthma). These were

*Now at the Postgraduate Medical School of London, Hammersmith Hospital.

carried out at routine clinical attendances without regard to the child's condition at the time.

All the asthmatic patients had had typical paroxysms of breathlessness and wheezing within the previous 12 months. Four of them produced small amounts of purulent sputum but were otherwise typical and severe examples of the condition.

All the patients with bronchiectasis had permanent cough with purulent sputum and persistent abnormal segmental shadows on plain radiographs of the chest; the presence of bronchiectasis had been confirmed by bronchography in 35 of them.

The ventilatory capacity in terms of the forced expiratory volume in one second (F.E.V.₁) had been found to be a satisfactory objective measurement of the severity of asthma in children (Strang, to be published). In order to compare this with the level of blood eosinophilia, a group of 14 children with asthma were seen as out-patients at 14-day intervals for a period of six months (182 examinations), when the F.E.V.₁ was measured and the eosinophils were counted. Though it was not anticipated in the plan, a number of attacks of clinical influenza occurred in these patients, and these events were recorded. The procedure for measuring the F.E.V.₁ was the same as described elsewhere (Strang, 1959). Eosinophil counts were done on ear-prick samples by the direct enumeration technique of Randolph (1944).

Comparison of Eosinophil Counts in Children with Asthma and Bronchiectasis

The initial eosinophil count performed on each child was regarded as a random observation, and therefore as a fair basis for comparison between children with asthma and those with bronchiectasis. The results (Fig. 1) show a large and obvious difference in the two groups with only a small overlap. Eosinophilia of over 600/c.mm. was present in 37 out of 43 patients with asthma, and

FIG. 1.—Initial eosinophil counts on 83 patients.

in none of 40 with bronchiectasis. A second count in 30 of the asthmatics failed to reveal an eosinophilia in only two.

The initial eosinophil counts on the four asthmatic children who had purulent sputum were 1,085, 2,175, 1,530, and 1,175/c.mm.

Serial Observations of Eosinophil Count and Ventilatory Capacity in 14 Children with Asthma

Serial observations showed that eosinophilia was very persistent in these patients. A typical record of eosinophil counts and F.E.V.s in one child is presented in Fig. 2.

Low counts were infrequent, a count below 350/c.mm. occurring on 11 occasions only. On seven of these it was recorded that the child was suffering from or just recovering from an illness regarded as influenza. In fact, the seven recorded infections occurred within a period of 28 days at a time when influenza B infections were known to be very common. Two of the four remaining low counts occurred during the same 28-day period.

A comparison of eosinophil counts and ventilatory measurements is presented in the Table. To allow comparison between children of different size the

FIG. 2.—Serial observations of F.E.V.₁ and eosinophils in one child (No. 12). + Signs indicate generalized rhonchi on auscultation.

F.E.V.₁ is expressed as a percentage of normal for height (Strang, 1959). The correlation between the eosinophil count and the F.E.V.₁ in the pooled results was not significant, nor between the individual mean values of eosinophils and F.E.V.₁. One child (No. 2) had a significant negative correlation, worsening of his asthma being associated with increasing eosinophil counts

Eosinophil Count (per c.mm.) + F.E.V.₁ (percentage normal) in 14 Asthmatic Children—Means, Standard Errors, and Correlations

No.	Mean Eosinophil Count (S.E.)	Mean F.E.V. ₁ (S.E.)	No. of Observations	Correlation Coefficient	P
1	943 (94)	51 (4.4)	11	+0.230	>0.05
2	770 (92)	56 (2.9)	15	-0.760	<0.05
3	668 (94)	82 (3.5)	13	+0.315	>0.05
4	645 (77)	65 (4.5)	13	+0.154	>0.05
5	804 (56)	67 (1.5)	15	+0.208	>0.05
6	549 (65)	76 (10.8)	13	-0.176	>0.05
7	1,596 (240)	115 (1.9)	12	+0.463	>0.05
8	1,072 (196)	79 (3.1)	11	+0.536	>0.05
9	1,097 (101)	39 (1.7)	12	+0.160	>0.05
10	713 (110)	61 (3.7)	13	+0.151	>0.05
11	893 (107)	36 (4.2)	13	+0.364	>0.05
12	1,072 (144)	66 (5.0)	14	+0.255	>0.05
13	1,191 (103)	40 (2.5)	14	+0.080	>0.05
14	1,235 (193)	58 (2.1)	13	+0.045	>0.05

Correlation coefficient for pooled results = +0.135 (n=182; P>0.05).
Correlation coefficient between mean values of F.E.V.₁ and eosinophil count = +0.175 (n=14; P>0.05).

However, the trend in the other children was in an opposite direction, the association being between increasing eosinophil counts and improvement. Indeed, 12 of the 14 correlation coefficients were of the same (positive) sign, and by the sign test this trend is significant at the 5% level. There was no obvious clinical difference between Case 2 and the other children, but if he were excluded the correlation coefficient for the remainder would be positive and significant ($r = +0.203$; $n = 167$; $P < 0.05$).

Discussion

Though the association of asthma and eosinophilia is well known, it is surprising to find that random eosinophil counts in a group of asthmatic children so often show abnormally high levels. That this state of affairs is not commonly recognized is revealed by a question published in the *Journal of the American Medical Association* (1955), which sought an explanation for persistent eosinophilia in a child with asthma. Two experts, in answering the question, regarded the finding as unusual and suggested investigations for parasitic infection.

In this material eosinophilia is very persistent in asthmatic children and in general is unrelated to the severity of the asthma. The trend, if anything, is the opposite of that expected, the higher levels of eosinophilia being associated with the better ventilatory performances.

By chance, marked falls in the eosinophil count were noted in response to apparent possibly influenzal infections. This observation should be extended by further observations on a variety of infections in asthmatics.

In children with bronchiectasis there is no evidence of an associated eosinophilia, and because of this the eosinophil count may help to differentiate the two conditions. This may be unnecessary in clear-cut examples, but, in fact, the clinical syndromes may overlap. Thus children with bronchiectasis have attacks of noisy breathing which have been described as wheezing (Field, 1949), and they can be shown frequently to have a ventilatory impairment associated with bronchial obstruction (Strang, to be published). In addition, the bronchial dilatations long regarded as the characteristic feature of the disease may be quite insignificant and unrelated to the extent of severity of bronchial damage (Whitwell, 1952). On the other hand, asthmatic children sometimes develop a persistent cough and sputum, which in a few of them is purulent. Both conditions probably include examples of early or potential chronic bronchitis, which may be a final common path for some of these children.

In any scientific study of bronchitis in children it would be very important to distinguish asthma from bronchiectasis or other categories. Eosinophilia appears to be a sufficiently constant feature of asthma to serve as a basis for such a differentiation.

Summary

Eosinophilia is common and very persistent in children with asthma. The height of the eosinophil count is unrelated to the severity of the condition as measured by the F.E.V.₁. The eosinophil count is not raised in bronchiectasis, and it may serve as a means of distinguishing these conditions in borderline cases and in scientific investigations of bronchitis in childhood.

Thanks are due to Professor S. D. M. Court for helpful criticisms, and to Dr. E. G. Knox and Mr. D. Newall for statistical advice.

REFERENCES

- Biggart, J. H. (1932). *J. Path. Bact.*, **35**, 799.
 Code, C. F. (1952). *Physiol. Rev.*, **32**, 47.
 Field, C. E. (1949). *Pediatrics*, **4**, 21.
J. Amer. med. Ass., 1955, **157**, 201.
 Randolph, T. G. (1944). *J. Allergy*, **15**, 89.
 Stickney, J. M., and Heck, F. J. (1944). *Med. Clin. N. Amer.*, **28**, 915.
 Strang, L. B. (1959). *Thorax*, **14**, 304.
 Urbach, E., and Gottlieb, P. M. (1946). *Allergy*, 2nd ed. Grune and Stratton, New York.
 Vaughn, J. (1953). *Blood*, **8**, 1.
 Whitwell, F. (1952). *Thorax*, **7**, 213.

DOG-BITES AND LOCAL INFECTION WITH PASTEURELLA SEPTICA

BY

M. L. H. LEE, B.M., F.R.C.S.

AND

A. J. BUHR, B.A., M.D.

From the Accident Service, Radcliffe Infirmary, Oxford

Dog-bites are common; we see over a hundred new patients with this injury in our accident service annually. The present investigation was carried out to examine the therapeutic management of dog-bites, and, in particular, bites infected with *Pasteurella septica*. Human *P. septica* infection following these bites is thought to be rare—only five cases have been recorded in this country (Allott *et al.*, 1944; Brunsdon and Mallett, 1953; Emson, 1957); we found 12 additional cases in a review of our records.

Present Investigation

Material.—The records of 69 patients (1952–7) who had suffered dog-bites which had been investigated bacteriologically were reviewed. (No bacteriological examination had been made of the wounds of the other patients who suffered dog-bites during this period.) Of this number, 39 were adults and 30 were children under 13 years of age. Swabs from 59 of these wounds were taken on the first day of attendance at hospital, as they were thought to be contaminated wounds. The remaining 10 were swabbed some days later, when it became apparent that a wound infection had developed. All swabs were cultured both by aerobic and by anaerobic methods.

Site of Injury.—The location of these bites was: face, 19 (17 children); upper limb 32 (8 children); lower limb, 18 (5 children).

Treatment.—Tetanus toxoid or antiserum was administered. No situation arose in which it was considered necessary to give antirabic serum or vaccine. Wounds were cleansed with a detergent and left unsutured in 39 instances in accordance with accepted practice. In 30 patients it was thought advisable to carry out excision and suture after careful wound toilet. Prophylactic penicillin therapy was given in only nine cases, in three of which the bite had been sutured; all these nine patients attended hospital on the day of injury.

Wound Infection.—Frank infection of wounds developed in 20 (29%) cases. Of the 17 children bitten on the face, five developed wound infection. Of the 30