Hypersensitivity to Some Nematode Antigens

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Summary

Immediate and delayed skin reactions to antigens derived from *Ascaris suum*, *Necator americanus*, and *Toxocara canis* are described in three subjects and related to eosinophil counts and serum IgE levels. One, who had laboratory contact with ascarides but no known infection, gave positive immediate reactions to all three antigens. Another, following repeated experimental infection with necator, gave positive immediate reactions to all three antigens and a delayed reaction to necator alone. The third, following a single recent infection with necator, gave no immediate or delayed reaction.

Introduction

It is hard to establish either the sensitivity or the specificity of diagnostic tests in nematode infections, since the timing and extent of exposure are seldom known, and most naturally infected people harbour more than one species of parasite. We have taken advantage of accurately known histories in three subjects to evaluate immediate and delayed skin sensitivity tests to extracts of *Ascaris suum*, *Necator americanus*, and *Toxocara canis*, and have related the results to eosinophil counts and serum IgE levels.

Patients and Methods

All three subjects were Englishmen. Subject A had had no known nematode infection. He had worked with *A. suum* for many years, and for some years had had asthma on exposure to the worms or extracts of them. His absolute eosinophil count was 160/mm³. Serum IgE was within normal limits (173 ng/ml). Subject B had been repeatedly infected with *N. americanus* over a period of five years, the last time being six months previously. His stools contained 25,000 ova/g. Repeated examinations had shown no other parasite. His eosinophil count was 2,070/mm³, and serum IgE was very high (7,359 ng/ml). Both had been normal before infection began. Subject C had had a single experimental infection with 25 *N. americanus* larvae six weeks earlier. His eosinophil count had risen during that period from 200 to 3,400/mm³. Serum IgE was normal (97 ng/ml). Subjects B and C had lived in the tropics for a time, but had had repeatedly negative stool examinations then and since.

The antigens used were a 1/10 w/v crude saline extract of whole adult *A. suum*, a 1/10 saline extract of third-stage larvae of *N. americanus*, both further diluted 1/10 in normal saline before use, and a 1/1,000 saline extract of adult *T. canis* prepared by the method of Woodruff and Thacker (1964) and used without further dilution. Each antigen was pricked through the skin of the flexor aspect of the left

forearm, together with a saline control. The resulting areas of induration and of erythema were read after half an hour and again at 48 and 72 hours. In addition, 0.1 ml. of *T. canis* antigen was injected intradermally into the right forearms of Subjects A and B, in conformity with the standard test described by Woodruff and Thacker (1964).

Results

The areas of the resulting induration and erythema are shown in the Table. Subject A had a very severe immediate reaction to all three antigens, but no delayed reaction. Subject B had positive immediate responses to all three antigens, but a delayed reaction to necator only. Subject C did not respond to any of the antigens.

Discussion

An apparent cross-reaction has been shown between immediate hypersensitivity to crude antigens derived from ascarides, necator, and toxocara. In addition, a subject recently infected with necator gave a negative response to homologous antigen, despite an eosinophilia, and after a period which has been shown to be sufficient for immediate hypersensitivity to have developed (Ball and Bartlett, 1969).

These findings suggest caution in the interpretation of both positive and negative responses to such tests. A positive response may not be specific to the parasite from which the antigen was prepared, and a negative response may indicate only that the infecting dose was below the threshold for the test, or that infection occurred too recently or too long ago. The specificity of the skin test may not be very important in practice when a nematode infection is suspected in a person who has not left Britain. The clinical picture of visceral larva migrans of *T. canis*, for example, is unlikely to be confused with that of other nematode infections, and in such a case the sensitivity of the test is critical.

The findings also have implications for the development of

Response to Antigens Pricked Through the Skin and to 0.1 ml. of *Toxocara* Antigen Injected Intradermally

		Erythema (cm ²)	Induration (cm ²)
Subject A			
Prick	‡ hour	Ascaris 8	0.4
		Necator 5.4	0.4
		Toxocara 6.1	0.3
		Control 0	0.02
Intradermal ‡ hour	48 hours	Indefinite induration and tenderness to all antigens	
	72 hours	All negative	
Subject B			
Prick	‡ hour	Ascaris 4.7	0.5
		Necator 2.3	0.4
		Toxocara 1.0	0.3
		Control 0	<0.01
Intradermal ‡ hour	48 hours	All negative	
		Ascarides 0	0
		Necator 0.15	0.15
		Toxocara 0	0
Subject C			
Intradermal ‡ hour	‡ hour	All negative	
	72 hours	All negative	

Subject A had asthma on contact with ascarides. Subjects B and C were infected with necator.

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diagnostic skin tests. All parasites may not necessarily produce as intense or as long-lasting an immediate hypersensitivity as does *T. canis* (Wiseman and Woodruff, 1970), and any trial of an antigen in subjects with different known infections should preferably include a direct comparison with their response to homologous antigen. This response cannot be predicted reliably from the presence of infection or on the evidence of the eosinophil count or serum IgE level.

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MEDICAL MEMORANDA

Duodenal Diverticulosis and Chronic Diarrhoea

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Two patients presented with persistent diarrhoea in association with vitamin-B₁₂ deficiency and duodenal diverticulosis. They are of practical interest in that the diarrhoea was greatly improved by parenteral vitamin-B₁₂ therapy alone, and are also of theoretical interest in that they throw further light on the mechanism of malabsorption that operates in the blind-loop syndrome.

Case 1

A man aged 61 suffered several attacks of pancreatitis over a two-year period and then had intermittent diarrhoea for the next five years. This progressed to continuous diarrhoea for two years, during which time he lost 30 lb (13.6 kg) in weight. The stools were pale, bulky, and offensive. The first attack of pancreatitis was confirmed by laparotomy. Subsequently, three episodes were diagnosed clinically. These were relatively mild, and on two occasions the patient was managed at home. Examination showed nothing abnormal apart from generalized wasting. Haemoglobin was 12.0 g/100 ml, and initial investigation revealed a megaloblastic anaemia. Serum vitamin-B₁₂ concentration was 55 pg/ml; serum folate 4.0 ng/ml; and red cells folate 190 ng/ml. The total fasting fatty acid concentration in the serum was 194 mg/100 ml. The levels after a fatty test meal were 176 mg/100 ml at two hours and 208 mg/100 ml at four hours. After two intramuscular injections of 1 mg of cyanocobalamin the diarrhoea gradually ceased and the haemoglobin rose to 14.3 g/100 ml. Four months later the diarrhoea returned, but responded to weekly injections of 1 mg of cyanocobalamin. After eight weeks the injections were reduced to once a month, but a further relapse occurred. Before treatment the serum proteins were 5.8 g/100 ml; after treatment they had risen to 6.5 g/100 ml. He returned to weekly injections and has remained well for six months.

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Comment.—Free acid in the stomach together with the absence of parietal cell antibodies in the serum excluded the diagnosis of pernicious anaemia. A "blind-loop syndrome" was suggested by the radiological finding of a large diverticulum arising from the descending duodenum (Fig. 1). Despite the history of recurrent pancreatitis a pancreozymin-secreatin test was negative. The stomach and intestines at the time of laparotomy were reported to be normal. The subsequent attacks consisted of pain in the right hypochondrium associated with generalized abdominal discomfort and diarrhoea. Pancreatitis is a known complication of duodenal diverticulosis.

Case 2

A woman aged 73 had passed up to 12 semiformed stools a day for 20 years. The diarrhoea was of a sudden onset and a diagnosis of colitis had previously been made. Her admission to hospital was precipitated by the loss of 14 lb (6.4 kg) in weight in association with anorexia, nausea, abdominal discomfort, and occasional

FIG. 1—Case 1. Radiological view of solitary duodenal diverticulum.