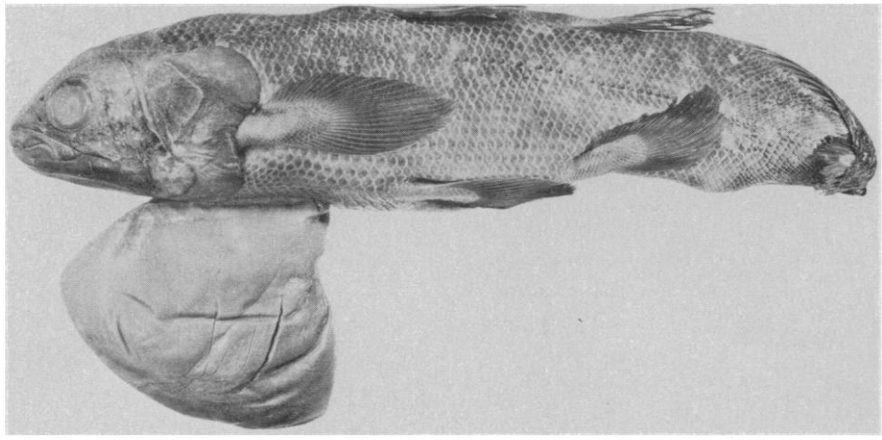

Fig. 2. Yolk-sac young of *Latimeria chalumnae*, the second of five found in a female 1.6 m long at the American Museum of Natural History. Unretouched photograph shows fins and tail as compressed by oviducal walls. Total length, 322 mm.

The specimen of *Latimeria* in the American Museum of Natural History measures 1.6 m in total length; its weight at the time of capture was reported to be 65 kg (*9*). The anatomy of the head of this specimen has been investigated (*10*), but its viscera were not dissected until recently, when samples of hemopoietic tissues were taken. During the course of the dissection, five advanced young were discovered lying free in the right oviduct. Millot and Anthony (*1, 2*) have observed that only the right oviduct is functional in *Latimeria*. As indicated in Fig. 1, all of the young were situated with their heads directed away from the urogenital orifice.

The following observations were made on four of the young that were removed from the oviduct, the fifth having been left in situ. The young resemble miniature adults, differing most noticeably in the possession of a yolk sac, the relatively larger eyes, and a more declivous profile (Fig. 2). Total length ranges from 301 to 327 mm, with an average of 317.8 mm. The maximum diameter of the yolk sac ranges from 80 to 129 mm; the largest fish has the smallest yolk sac, and vice versa. The yolk-sac stalk is broad, extending from the base of the pectoral fins approximately two-thirds of the distance to the base of the pelvic fins. Scales and fins appear to be fully developed in all four young, but they lack the denticles (odontodes) of the adult.

The gravid female under discussion was caught in January, the same month in which females with ovulated eggs have been taken. This suggests that gestation may require more than a year—not an unexpected length of time in view of the tremendous size of the ripe egg.

Millot and Anthony (*1*) showed that the male of *Latimeria* possesses a cloaca which contains a urogenital papilla and is flanked externally by two pairs of erectile caruncles. Since internal fertilization of the female must occur, it seems likely that the cloaca functions as an eversible copulatory organ, in a manner reminiscent of the situation in some birds and gymnophiones (*11*). The caruncles perhaps serve as claspers. Similar suggestions have been made by Griffith and Thomson (*6, 12*).

Paleoichthyologists usually consider the coelacanths to be most closely related to the Paleozoic rhipidistians, and the latter in turn to be the fishes most closely related to the tetrapods (*13*). Nothing is known about reproduction in the rhipidistians, and there is no way of knowing whether the ovoviviparous condition in *Latimeria* is unique or whether it is shared by other crossopterygians and primitive tetrapods. Among other major groups of bony fishes, living lungfishes are oviparous, as are all living actinopterygians except 11 families (less than 5 percent) that exhibit viviparity or ovoviviparity as a derived condition or specialization. Although the ovoviviparity of *Latimeria* sheds no light on the reproductive mode of primitive osteichthyans, including crossopterygians, it does indicate that all the information we now have about reproduction in the fossil coelacanths is consistent with the hypothesis that they were ovoviviparous.

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12. In the light of the present discovery, Griffith and Thomson also may have been correct in suggesting that the isolated yolk-sac larvae described by Schultze were prematurely released from a stressed female. Such behavior is often seen in ovoviviparous sharks, rays, and teleosts.
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Immunoglobulin E Antibodies to Pollen Allergens Account for High Percentages of Total Immunoglobulin E Protein

Abstract. *The quantities of immunoglobulin E (IgE) antibodies to grass or ragweed allergens were measured by an immunoabsorption in the serums of patients sensitive to one of these allergens. IgE antibodies to grass or ragweed allergens accounted for means of 30 and 29 percent of the total IgE protein. After the ragweed pollination season, the levels of serum IgE antibodies to ragweed allergens rose dramatically and in postpollination serums they accounted for 39 percent of the total IgE protein with a range from 13 to 50 percent.*

IgE antibodies are responsible for the typical wheal and flare reactions induced in the skin of allergic individuals by injection of specific allergens (*1*). This activity may be transferred by serum to the skin or the leukocytes of normal subjects and may be measured by testing serum dilutions (*2*). The activity of IgE antibodies may also be measured in vitro more simply by the radioallergosorbent test (RAST) (*3*). In this procedure allergens linked to solid phase supports are incubated with serum from allergic subjects.

IgE antibodies bind to the solid phase allergen and they are detected by addition of isotopically labeled antibodies to IgE.

Analysis of the stoichiometry of the steps in the RAST indicates that IgE antibody to the allergen is in excess in the first step of the test (*4*). Therefore, there must be competition among antibodies for allergenic determinants, and the final measurement is a function of both the quantity and the affinity of the IgE antibodies. Thus, RAST provides a measure of the activity of IgE antibodies and not of their quantity in weight units. In our study we have determined the absolute quantities of IgE antibody to grass and ragweed allergens by immunoabsorption. We selected this approach because in previous studies we had found that the total amount of IgE protein may rise dramatically in certain subjects after the ragweed pollination season, suggesting that a considerable quantity of the IgE protein is antibody to ragweed antigens (*5*).

Initially we analyzed 14 serums from patients with allergic rhinitis who were clinically sensitive to either grass or ragweed (*6*). None of the patients was receiving therapeutic pollen injections. In all the serums IgE antibodies to either grass or ragweed were increased, as judged by the RAST. The RAST reactivity was removed by the homologous allergen and not by the control immunoabsorbents (*7*). The IgE levels in the serums of the patients sensitive to grass were lowered by exposure to the grass and not to the human serum albumin (HSA) or ragweed immunoabsorbents (Table 1). In contrast the IgE in the serums of the ragweed-sensitive patients were lowered by exposure to the ragweed and not to HSA or grass immunoabsorbents. No difference was found between the IgE levels in the serums treated with the control allergen and the HSA immunoabsorbents. The quantity of specific IgE antibody was the difference in the IgE protein levels between the control and the test values and averaged 30 and 29 percent of the total IgE protein in the grass and ragweed serums, respectively.

To determine the magnitude of the rises in IgE antibody levels in ragweed-sensitive patients, we analyzed serums from ten subjects in July, before the onset of the pollination season and again in late September or October when the IgE antibody activity had reached a maximum (*8*). Samples of these serums were tested with a ragweed immunoabsorbent and all of the IgE antibodies reactive with ragweed antigens as measured by the RAST were removed. As a control, another sample of the same serum was absorbed with the HSA immunoabsorbent (Table 2). First, the quantity of IgE antibody found in serum obtained before the ragweed pollination season varied from 31 to 728 ng/ml; in one patient, no IgE antibody was detectable by the absorption procedure. In these preseasonal serums IgE antibody accounted for 17 to 52 percent of the total IgE with a mean of 29 percent. Second, total IgE protein often increased strikingly in patients after the ragweed pollination season. For example, patients 4 and 9 show more than fourfold rises, and patients 6 and 10 show more than twofold increases in total IgE protein. Similarly the concentrations of IgE antibodies also rose by as much as fivefold in one patient and they increased in all ten. In most cases, the percentage of the total IgE that could be accounted for as IgE antibody to ragweed also rose and the postseasonal mean for this value was 39 percent. Specific IgE antibody accounted for 27 to 113 percent of the rise in IgE protein with a mean of 61 percent.

These results provide unambiguous determinations of the quantities of IgE antibodies to ragweed and grass allergens in the serums of sensitive subjects and indicate that in these serums IgE antibodies account for high percentages of the total IgE protein. The percentages found are similar to those reported by Schellenberg and Atkinson (*9*) but higher than those

Table 1. Quantities of IgE antibodies to pollen allergens. Serum samples were absorbed with the test solid phase allergen to which the patient was sensitive, either grass-Sepharose or ragweed-Sepharose, and with two control immunoabsorbents, HSA-Sepharose and the other solid phase allergen to which the patient was not sensitive. The IgE in the patient's untreated serum served as a third control. The quantity of IgE antibody to the allergen is the difference between the IgE protein concentration in the controls and in the serum absorbed with the test allergen. The percentages are the levels of IgE antibody divided by the control value × 100. For example, in patient 1 the difference between the IgE level in the unabsorbed serum and the serum absorbed with grass-Sepharose was 144 ng/ml. This represents 48 percent of the total IgE protein in the unabsorbed serum. The IgE protein was determined by radioimmunoassay (*18*); the coefficients of variation for the determinations in Tables 1 and 2 were 11.2 and 12.9 percent, respectively. Two samples of each serum were tested with the various immunoabsorbents, and the supernatants were analyzed for IgE in two separate radioimmunoassays at two different concentrations. Thus the values in the table are the means of a minimum of six and usually eight determinations.

Sample	IgE (ng/ml)				IgE antibodies as percent of total IgE protein		
	Serum unabsorbed	Serum absorbed with			Serum unabsorbed	Serum absorbed with	
		HSA-Sepharose	RW-Sepharose	Grass-Sepharose		HSA Sepharose	Control allergen-Sepharose
			Grass-sensitive patients				
1	300	266	249	156	48	41	37
2	599	587	518	336	44	43	35
3	198	242	258	207	−5	15	20
4	233	279	282	220	6	21	22
5	566	574	538	455	18	21	15
6	830	781	842	508	39	35	40
7	459	432	424	237	48	44	44
			Ragweed-sensitive patients				
8	3044	2965	2201	3182	28	26	31
9	8952	7350	7350	8921	18	0	18
10	671	584	286	597	57	49	52
11	388	437	256	460	34	41	44
12	216	257	187	260	13	27	28
13	1716	1650	1404	1868	18	15	25
14	922	847	629	851	32	26	21

Table 2. Seasonal rises in IgE antibodies to ragweed allergens.

Patient	Prepollination			Postpollination			Rise in IgE antibody (ng/ml)	Rise in IgE protein (ng/ml)	Antibody as percent of rise in IgE protein
	IgE antibody (ng/ml)	Total IgE (ng/ml)	Antibody (%)	IgE antibody (ng/ml)	Total IgE (ng/ml)	Antibody (%)			
1	261	804	33	546	1159	47	285	355	80
2	154	451	34	268	634	42	114	183	62
3	250	1189	21	340	1528	22	90	339	27
4	60	218	28	401	903	44	341	685	50
5	*	684		78	605	13	78	−79	
6	31	89	35	105	226	46	74	137	54
7	103	213	48	168	375	45	65	162	40
8	163	938	17	331	1087	30	168	149	113
9	323	616	52	1231	2671	46	908	2055	44
10	728	3147	23	3255	6451	50	2527	3304	76

*No difference found by absorption procedure.

found by Zeiss *et al.* (*10*), who showed in 15 patients that a mean of 13 percent of IgE protein was antibody to ragweed antigen E. However, Zeiss *et al.* used an indirect binding method to measure IgE antibody and only dealt with one of the allergens in ragweed pollen. Even so, in one patient 41 percent of IgE protein was antibody. Earlier Ishizaka and his associates, using a similar binding method, had suggested that a high percentage of IgE protein possessed antibody activity (*11*).

Few studies of this type have been conducted in experimental animals or man. In rabbits, after repeated injections of large quantities of bacterial or protein antigens, up to 90 percent of the gamma globulin may be accounted for as antibody (*12*). Usually, however, only 10 to 20 percent of rabbit immunoglobulin G possesses antibody activity even after immunization with adjuvants (*13*). In humans, immunization with dextran results in low levels of antibody which probably accounts for no more than 2 percent of the total immunoglobulin (*14*). Bandilla *et al.* immunized humans with hemocyanin, and their results indicate that less than 2 percent of the IgG and IgA and 4 percent of IgM classes could be accounted for as antibody during a secondary response (*15*). Our finding that IgE antibody accounts for such high percentages of total IgE protein presumably reflects the local deposition of pollen in the nose and the presence in nasal tissues of relatively large numbers of IgE-producing plasma cells (*16*). Finally, the demonstration that IgE antibody accounts for such a high percentage of the total IgE protein should stimulate further studies of means to depress these levels, especially because the severity of ragweed hay fever can be related to the level of IgE antibody (*17*).

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6. These serums were selected from among those analyzed routinely for IgE antibodies by the RAST in the clinical laboratory and contained IgE antibodies to either ragweed or grass allergens. The reactivity of the serums from the grass-sensitive patients in the RAST ranged from 6 to 25 percent and for the serums from the ragweed-sensitive subjects from 5.4 to 41.1 percent. These values are comparable to those among unselected patients with allergic rhinitis due to grass or ragweed pollen. Finally, these patients had positive skin tests to a variety of allergens suggesting that multiple sensitivities existed.
7. The immunoabsorbents were prepared by activation of Sepharose 2B (Pharmacia) with cyanogen brom → [R. Axen, J. Porath, S. Ernback, *Nature (Lond.)* **214**, 1302 (1967); J. W. Yunginger and G. J. Gleich, *J. Allergy Clin. Immunol.* **50**, 109 (1972)], and reaction with human serum albumin (HSA) (Fraction V; Sigma), partially purified ragweed extract [G. J. Gleich, J. B. Larson, R. T. Jones, H. Baer, *J. Allergy Clin. Immunol.* **53**, 158 (1974)] or rye grass extract. Three 30-ml samples of activated Sepharose 2B were reacted with 300 mg of HSA, 300 mg of rye grass extract, or 340 mg of ragweed extract at 4°C with tumbling for 24 hours. After thorough washing, 47 percent of the HSA was coupled (235 μg per milligram of Sepharose 2B), 52 percent of the rye grass extract was coupled (240 μg per milligram of Sepharose 2B), and 68 percent of the ragweed was coupled (387 μg per milligram of Sepharose 2B). The immunoabsorbents (6 mg) were added to serum samples, and 0.1*M* phosphate buffer ($K_2H_2PO_4$ and KH_2PO_4) (*p*H 7.4) containing 1 percent bovine serum albumin and 0.1 percent sodium azide was added to a volume of 2.0 ml. After rotation at room temperature for 3 days, the tubes were centrifuged, and the supernatants were analyzed for IgE protein by radioimmunoassay and for IgE antibody activity by RAST. In every case, all IgE antibody activity was removed by the immunoabsorbent containing the allergen to which the patient was sensitive.
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Infectious Etiology of Neuritic (Senile) Plaques in Mice

Abstract. *Brains of inbred female VM mice infected with scrapie agent were studied with the use of the Bodian silver impregnation method and by electron microscopy. In brains affected with scrapie, after an incubation period of between 587 and 655 days, numerous primitive, classical, and amyloid plaques were found. No plaques of any type were seen in the control mice.*

Neuritic (senile) plaques are the most conspicuous pathological changes found in people with Alzheimer's disease and senile dementia. They are also commonly found in middle-aged patients with Down's syndrome and, in smaller numbers, in a high percentage of normal old people (*1*) and have also been found in aged dogs and monkeys (*2, 3*). Morphological studies of neuritic (senile) plaques have revealed that they consist of degenerative neuronal processes, reactive cells, and amyloid, but the cause of their formation remains unknown. Here, on the basis of silver impregnation and electron microscopic studies, we report that neuritic plaques of both the classical and primitive types occur in mice in association with infectious disease.

The recent studies of Bruce and Fraser (*4, 5*) demonstrated plaques containing amyloid in the brains of mice that are infected with some strains of scrapie agent. Scrapie is a naturally occurring disease of sheep and goats that is caused by a replicating agent that can be transmitted with infected tissues to a variety of species. Morphologically, scrapie is often accompanied by vacuolar degeneration that may include a severe spongy change. Dickinson and Fraser (*6*) showed that there are different strains of scrapie agent that are distinguishable on the basis of incubation period and topography of the brain lesions in inbred mice. In the studies of Bruce and Fraser (*5*), with certain combinations of agent and mouse strains, plaques were seen in more than 70 percent of the brains of mice that were killed with the clinical disease, but not in a large number of control mice that were more than 600 days old. In Masson's trichrome preparations, the appearance of these plaques differed in certain details from neuritic (senile) plaques, although, ultrastructurally, all of the characteristic features of neuritic plaques were recognized. We report a further study of representative samples of severely affected mouse brains and control brains of comparable and greater age (some more than 1000 days) in which we used Bodian's silver impregnation technique and electron microscopy.

Four mice affected with scrapie that were known to have large numbers of amyloid plaques were examined. These were inbred female VM mice 610 to 705 days old. Two were infected with 87A scrapie agent, one with 125A, and the fourth with 51C. These agents were originally isolated from cases of natural scrapie in sheep; 87A was from a Border Leicester–Cheviot cross, 125A was from a Southdown, and 51C was