

Emerging Eosinophilic (Allergic) Esophagitis

Increased Incidence or Increased Recognition?

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• **Context.**—Eosinophilic esophagitis is a disease of the esophagus with distinct histologic features (prominent intraepithelial eosinophils, particularly superficial with clustering) and characteristic endoscopic features (trachealization, white plaques). The presence of intraepithelial eosinophils had been recognized since 1982 as indicative of reflux esophagitis but little attention was initially paid to their numbers or location. Eosinophilic esophagitis has been recently described and there have been a number of reports that its incidence is on the rise. It had been our impression that eosinophilic esophagitis was being seen more frequently, perhaps resulting from some environmental change.

Objective.—To investigate the increased prevalence of eosinophilic esophagitis.

Design.—We analyzed a similar group of cases from 2005 (n = 150) as compared with 1990 (n = 115). Con-

secutive patients with mucosal esophageal biopsies from May through June of the respective years were included in the analysis. Patients with Barrett metaplasia or with carcinoma were excluded. The highest density of intraepithelial eosinophils for each patient was recorded as the number of intraepithelial eosinophils per single high-power field. The patients were categorized by the number of intraepithelial eosinophils per high-power field with those cases with greater than 20 intraepithelial eosinophils per high-power field representing eosinophilic esophagitis.

Results.—There was no difference in the incidence of eosinophilic esophagitis between 1990 and 2005.

Conclusions.—The apparent increased incidence of eosinophilic esophagitis is largely a result of an increase in recognition rather than an increase in disease resulting from an environmental factor.

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Eosinophilic esophagitis (EE) tends to be a disease of young males characterized by symptoms of dysphagia, normal esophageal pH, history of allergy, poor response to acid blockade, and occasionally peripheral eosinophilia.^{1–3} Eosinophilic esophagitis has distinct histologic features (prominent intraepithelial eosinophils [IEEs], particularly superficial with clustering) and characteristic endoscopic features (trachealization, white plaques).³ The presence of IEEs had been recognized since 1982 as indicative of reflux esophagitis (RE) but little attention was initially paid to the numbers or location of eosinophils.⁴ Eosinophilic esophagitis was first described in the mid 1990s,^{5,6} and there have been a number of recent reports that its incidence is on the rise.^{7–9}

There is clear evidence that substantial numbers of IEEs in esophageal biopsies are linked with the clinical presentation of EE and refractoriness to acid blockade. Recent publications have, in general, used a cutoff of more than 20 to 24 IEEs/high-power field (HPF) for the diagnosis of EE.^{7,8} A study correlating number of IEEs per HPF with acid reflux index found that more than 20 IEEs/HPF is

associated with a normal reflux index and a nonacid-related cause of esophagitis.¹⁰

It had been our impression that EE was being seen more frequently. It was hypothesized that this was perhaps resulting from some environmental change, such as the

Table 1. Summary of the Number of Cases Found in Each Category of Intraepithelial Eosinophils per High-Power Field (IEEs/HPF) From 1990 and 2005*

	IEEs/HPF				Total Cases
	0	1–9	10–19	≥20	
1990	67 (58)	39 (34)	1 (1)	8 (7)	115 (100)
2005	79 (53)	57 (37)	4 (3)	10 (7)	150 (100)

* The percentage of the total number of cases evaluated from that year is given in parentheses.

Table 2. Summary of the Number of Intraepithelial Eosinophils per High-Power Field (IEEs/HPF) Comparing Reflux Esophagitis and Eosinophilic Esophagitis in 1990 and 2005

	IEEs/HPF		
	Range	Mean	Median
Reflux esophagitis			
1990	1–11	3	2
2005	1–18	3	1
Eosinophilic esophagitis			
1990	26–156	51	37
2005	21–139	56	39

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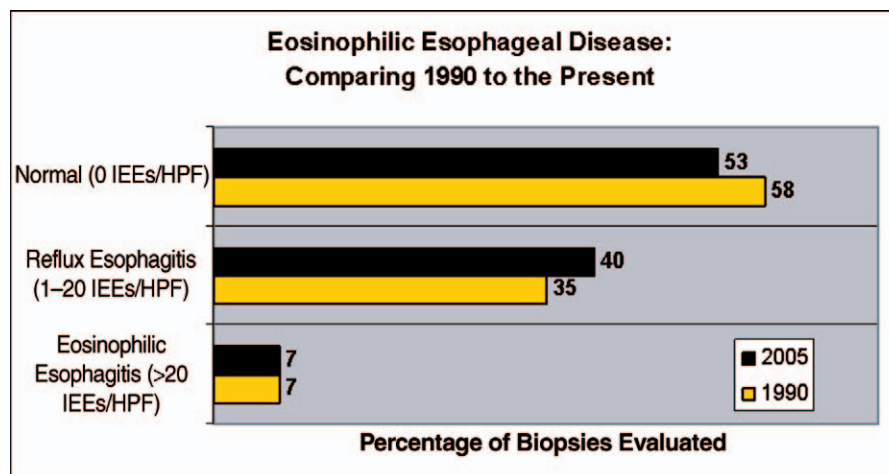
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Figure 1. Eosinophilic esophageal disease: comparing 1990 to the present (2005). The graph shows the percent of biopsy evaluated from the respective years, which were determined to represent normal, reflux esophagitis, and eosinophilic esophagitis. IEE indicates intraepithelial eosinophil; HPF, high-power field.

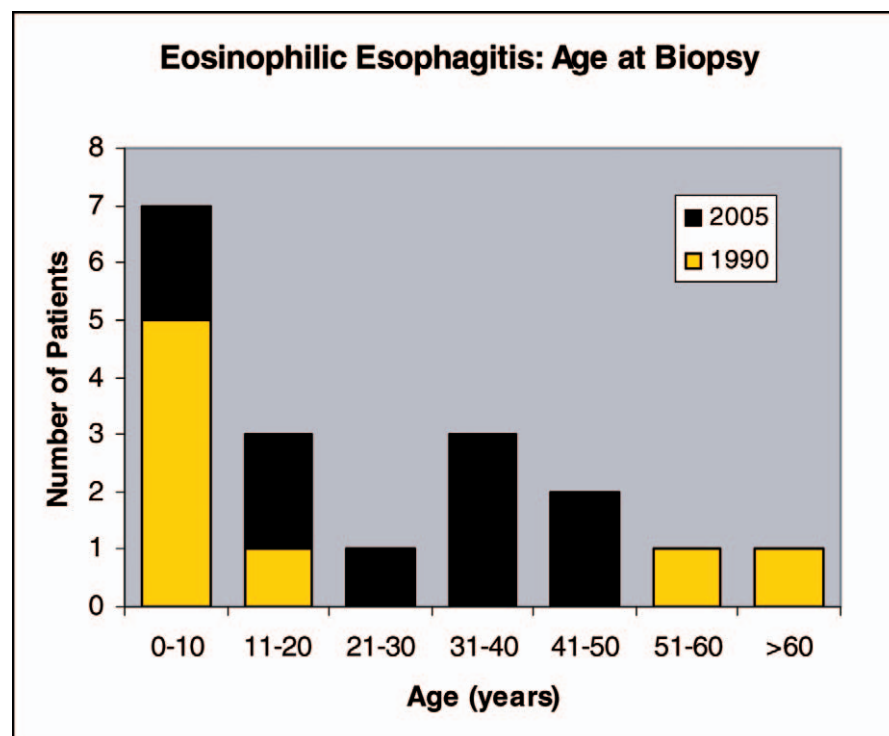


widespread use of proton pump inhibitors in recent years compared with the past use of histamine 2 blockers.

DESIGN

We analyzed a similar group of cases from 2005 ($n = 150$) as compared with 1990 ($n = 115$) through a protocol approved by the University of Iowa institutional review board. Consecutive patients with mucosal esophageal biopsies from May through June of the respective years were included in the analysis. Patients with Barrett metaplasia or with carcinoma were excluded. The highest density of IEEs for each patient was recorded as the number of IEEs per single HPF. In addition, the presence of superficial IEEs and aggregates of IEEs were noted. The patients were categorized by the number of IEEs per HPF with those cases with greater than 20 IEEs/HPF representing EE, 1 to 20 IEEs/HPF representing RE, and 0 IEEs/HPF representing normal biopsies.

Figure 2. Eosinophilic esophagitis: age at biopsy. The graph shows the number of patients in each decade of life with the histologic diagnosis of eosinophilic esophagitis.



RESULTS

There was no difference in the incidence of EE between 1990 and 2005 (Figure 1). All biopsies with greater than 20 IEEs/HPF also contained the associated features of superficial IEEs and aggregates of IEEs. No biopsies with less than 20 IEEs/HPF had both superficial IEEs and aggregates of IEEs. The numbers of cases in each category (with corresponding percent of total cases evaluated from that year) are shown in Table 1.

The numbers of IEEs seen in RE was similar between the 2 timeframes with an average of 3 IEEs/HPF with most cases having 1 or 2 IEEs/HPF. Likewise the numbers of IEEs were similar in EE comparing across years with an average of around 50 IEEs/HPF. The breakdown of IEEs per HPF for RE and EE is shown in Table 2.

Of the 18 total patients identified as meeting the histologic criteria for EE, there was a male-female ratio of 3.5:1. The age distribution at biopsy is shown in Figure 2.

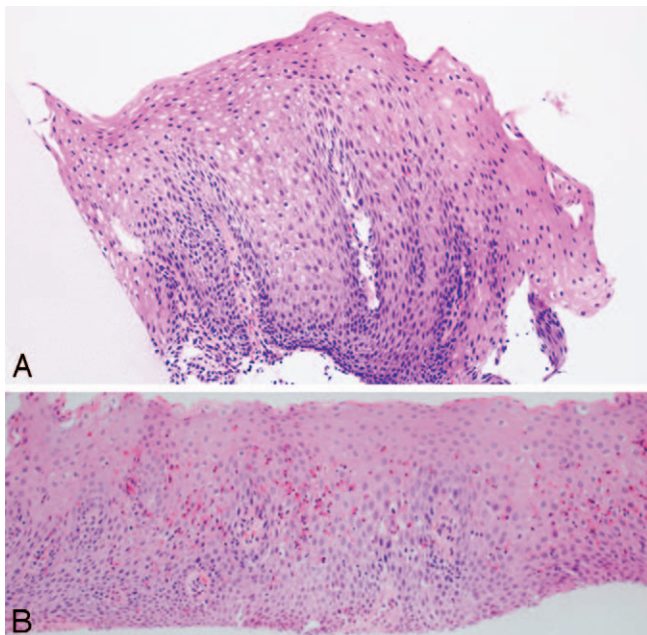


Figure 3. A, Reflux esophagitis shows papillary lengthening, basal hyperplasia, and rare intraepithelial eosinophils (IEEs) (hematoxylin-eosin, original magnification $\times 20$). B, Eosinophilic esophagitis shows prominent IEEs, aggregates of eosinophils, and superficial eosinophils (hematoxylin-eosin, original magnification $\times 20$).

CONCLUSION

The demographics of the patients identified with EE in this study agree with the previously held notion that EE is a disease of young males, with a 3.5:1 male-female ratio and a pediatric predominance. Also, there was a close correlation between identifying superficial IEEs and aggregates of IEEs with finding greater than 20 IEEs/HPF and an ultimate histologic diagnosis of EE. This may be a helpful diagnostic criterion for the rare borderline case to distinguish EE (Figure 3, B) from RE (Figure 3, A).

One possible confounding factor is whether the recent increase in clinical recognition of EE has lead to an increase in biopsies in patients fitting the typical clinical profile. This could possibly lead to an increase in biopsies of these patients with an endoscopically normal appearing esophagus in 2005 as compared with 1990. The total number of endoscopies performed during the time periods was not available to address this issue. If anything, this decreased awareness and tendency not to biopsy in 1990 may have lead to underrepresentation of EE in our study during that time period.

The perceived increase in EE at our institution was not validated on comparing biopsies from 1990 and 2005. Therefore, it is concluded that the apparent increased incidence of EE is largely a result of an increase in recognition rather than an increase in disease resulting from an environmental factor.

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