

Excess Autoimmune Disease Mortality Among School Teachers

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ABSTRACT. Objective. To investigate evidence of an association between school teaching and mortality from autoimmune diseases.

Methods. A proportional mortality study using US death certificates from the 1985-95 period was conducted. Death certificates that listed elementary or secondary school teaching as the usual occupation were identified, as were those that cited any of 13 autoimmune diseases as a cause of death. Proportional mortality ratios (PMR) were calculated to compare autoimmune disease mortality among teachers to that among persons in other professional occupations.

Results. The PMR for total autoimmune disease mortality among teachers was 113 ($p < 0.0001$). Rheumatic diseases accounted for 53.1% of the total excess in mortality and multiple sclerosis accounted for 39.9%. Significantly elevated autoimmune disease mortality occurred for female teachers (PMR = 111, $p < 0.0001$), male teachers (PMR = 124, $p < 0.0001$), white teachers (PMR = 112, $p < 0.0001$), non-white teachers (PMR = 118, $p = 0.005$), elementary teachers (PMR = 111, $p < 0.0001$), and secondary teachers (PMR = 130, $p < 0.0001$). There was an inverse trend ($p < 0.0001$) in the level of excess mortality relative to age. PMR were 149, 144, 127, 118, 108, and 102 for teachers in the 35-44, 45-54, 55-64, 65-74, 75-84, and ≥ 85 year age groups, respectively. Excess mortality was significantly greater in secondary teachers than elementary teachers both in total (PMR = 112, $p = 0.04$) and in the 35-44 age group (PMR = 155, $p = 0.03$).

Conclusion. Our results substantiate excess mortality from autoimmune diseases among teachers and suggest that, relatively early in their careers, teachers experience an occupational exposure that increases risk of autoimmune diseases. (J Rheumatol 2001;28:1537-45)

Key Indexing Terms:

AUTOIMMUNE DISEASES EPIDEMIOLOGY OCCUPATIONS MORTALITY

Autoimmune diseases are those in which the immune system attacks normal body tissues as foreign antigens. More than 60 diseases may result from autoimmune processes¹. Environmental factors are believed to contribute to their pathogenesis². Case reports and epidemiological studies suggest a role for occupational exposures in the etiology of rheumatoid arthritis (RA), scleroderma, and systemic lupus erythematosus (SLE)³⁻⁵.

The US National Institute of Occupational Safety and Health (NIOSH) initiated the National Occupational Mortality Surveillance system (NOMS) in 1979⁶⁻⁸. NOMS monitors associations between occupation and disease by collecting data from death certificates pertaining to usual occupation, industry of employment, and cause of death. A comprehensive survey based on NOMS data was published

by NIOSH in 1997⁹. Complete results of the survey can be accessed through the Internet⁷.

One occupational classification evaluated in the NIOSH survey was "teaching, except post-secondary." Among white female decedents in this classification, significant excess mortality was noted for a number of cause of death categories that include autoimmune diseases: diffuse diseases of connective tissue, diseases of musculoskeletal system and connective tissue, multiple sclerosis and other demyelinating diseases, rheumatic fever and heart disease, and RA and other inflammatory polyarthropathies. The survey also found excess mortality from all but the last of these categories among white females whose industry of employment was listed as "elementary and secondary schools." White females employed in that industrial classification also experienced excess mortality from "polyarteritis nodosa and allied conditions." Among black females, teaching as the usual occupation was associated with elevated mortality from diffuse connective tissue diseases. Among white males, teaching was associated with excess mortality from multiple sclerosis.

The NIOSH survey did not investigate an extensive range of individual autoimmune diseases nor did it evaluate autoimmune diseases as a single, aggregated class. Although published in 1997, the survey was limited to data from an

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earlier 5 year period (1984-88). It did perform statistical adjustment for potential confounding by age and stratified results by sex and race, but it did not attempt to control for the effects of socioeconomic status usually associated with occupation. The survey searched for evidence of excess mortality from 192 disease categories across 325 occupational and 235 industrial classifications. This raises the possibility that, through a multiple comparisons phenomenon, many associations reported to be statistically significant reflect only random variation as opposed to true relationships¹⁰. The survey utilized only data on underlying cause of death. This is problematic in that diseases that are frequently listed as contributing causes (e.g., RA¹¹) may be undercounted. Further, as a study of proportional mortality, variation between occupations in the citation of common diseases as the underlying cause (e.g., via a healthy worker effect in some occupations) may artificially inflate or deflate the frequency with which less common diseases are cited as the underlying cause¹²⁻¹⁴. Such a phenomenon can result in measures of occupation-disease associations that do not reflect the real effects of occupational exposure on risk of mortality.

We used NOMS data to study mortality from autoimmune diseases among teachers in a more focused, complete, and rigorous fashion than was possible in the NIOSH survey. The broad goal was to validate the existence of excess autoimmune disease mortality among teachers. Specific goals were: (1) to study mortality from a wider spectrum of autoimmune diseases both in aggregate and separately; (2) to use all years of data available from NOMS; (3) to control potential confounding by age, sex, race, and socioeconomic status; (4) to concentrate only on autoimmune disease mortality among teachers in order to limit the number of statistical comparisons; and (5) to refer to both underlying and contributing causes of death in order to identify as much "autoimmune disease related" mortality as possible and to reduce the possibility of biased measures of association.

MATERIALS AND METHODS

The National Center for Health Statistics (NCHS) maintains a database of all death certificates filed in the United States. The database includes demographic information, an underlying cause of death, and multiple contributing causes for each decedent. Up to 19 contributing causes can be listed, but for most decedents the number is between one and 3. Causes of death are recorded using codes from the International Classification of Diseases, 9th revision (ICD)¹⁵.

In 1985, NCHS began to incorporate occupational information from NOMS into the mortality database. Occupational data are derived from the "usual occupation" field of the standard US death certificate. Occupations are categorized and coded using the Classified Index of Industries and Occupations (CIO)¹⁶. At the time this study was initiated, data were available for an 11 year period (1985-1995). Twenty-five states contributed occupational information to the mortality database during at least one year in that period.

Magnetic tapes storing the mortality database were read using SAS data management software (SAS Institute, Cary, NC, USA). All decedents in

states participating in NOMS during the 1985-95 period were identified subject to 2 criteria: (1) decedents from a state were included only for those years in which the state contributed data to NOMS, and (2) decedents were included only if their state of residence and state of occurrence of death both participated in NOMS during the year of death. The sex, race, age, occupation, underlying cause of death, and all contributing causes were recorded for each decedent who met the inclusion criteria. Only deaths in persons over age 25 years were included under the assumption that some degree of exposure time after college graduation and entry into the teaching profession would be necessary before the effects of increased mortality, if any, occurred.

Jacobson, *et al* recently characterized 24 diseases as having "direct, indirect, or strong circumstantial evidence" of autoimmune pathogenesis¹⁷. Among these, we chose to study diseases that satisfied 2 criteria. The first was that a disease must have the capacity to cause or contribute to mortality. The second was that a disease either have a unique ICD code or code range or that it substantially dominate all mortality attributed to the ICD code or code range that includes it. Thirteen diseases met these criteria: Addison's disease (ICD code 255.4); autoimmune hemolytic anemia (283.0); glomerulonephritis (580.0-583.9); Graves' disease (242.0); multiple sclerosis (340); myasthenia gravis (358.0); myocarditis (130.3, 422.0, 422.9, 429.0); polymyositis and dermatomyositis (710.3, 710.4); rheumatic fever and heart disease (390-398.9); RA (714.0-714.2); scleroderma (710.1); Sjögren's syndrome (SS 710.2); and SLE (710.0).

Deaths that listed either elementary or secondary school teaching as an occupation were identified. The CIO codes for these occupations are 156 and 157, respectively. Autoimmune disease mortality among teachers was compared to that in a control group consisting of deaths in all other professional occupations. The control group was limited to other professional occupations to compare teachers to a group of decedents with similar socioeconomic status. Occupations were deemed to be "professional" based on classification by the Bureau of the Census¹⁶. CIO codes for professional occupations fall in the range from 3 to 199.

Expected counts of autoimmune disease deaths among teachers were calculated based on proportional mortality in other professional occupations¹⁸. Expected counts were adjusted for differences in the distributions of age, sex, and race between teachers and other professionals, as appropriate. Observed mortality among teachers was compared to expected mortality using proportional mortality ratios (PMR). PMR were multiplied by a factor of 100 to express comparisons on a percentage scale. Confidence intervals and 2 tailed p values for PMR were calculated using the method of Byar for ratios based on Poisson counts^{19,20}. Tests for a trend in PMR relative to age were performed using the method of Armitage²¹. A 5% level of significance was applied in all statistical tests.

Analyses were conducted using data from the 1985-95 period. Analyses were repeated to investigate mortality from individual autoimmune diseases and to evaluate mortality among elementary and secondary teachers separately and relative to each other. Another set of analyses was restricted to data from the 1989-95 period. This shorter period was of interest to confirm that the patterns of autoimmune disease mortality among teachers during the 1985-95 period did not depend solely on data from the 1985-88 period included in the NIOSH survey.

RESULTS

Description of the study sample. There were 6,490,673 deaths among residents of states participating in NOMS during the 1985-95 period. Among these, 261,621 occurred in persons under age 25 and 923 occurred in persons of unknown age. Another 167,310 decedents, although residents of NOMS states, died in states that were not participating in NOMS. Among the remaining individuals, 100,678 did not have an occupation listed on the death certificate, 42,216 had "Retired" listed as their usual occu-

pation, and 75,393 were categorized as “Unemployed, disabled, or never worked.” Following these exclusions, 5,842,532 decedents remained whose usual occupation could be classified as either professional or non-professional. Of these, 860,648 were cited as having engaged in a professional occupation. This group constituted the study sample.

Crude proportional mortality among teachers. School teaching was listed as the usual occupation for 143,553 of the decedents with a professional occupation (Table 1). At least one of the 13 autoimmune diseases was cited as an underlying or contributing cause for 3,259 (2.3%) of these individuals. The proportion of deaths citing an autoimmune disease was higher among female teachers (2.4%) than among males (1.6%) and was higher among non-white teachers (2.6%) than among whites (2.2%). The highest proportion of autoimmune disease deaths occurred in the 35–44 year age interval (4.1%). There was a trend to lower proportions of autoimmune disease mortality across the older age groups.

Crude proportional mortality, teachers versus other professionals. Unstandardized total proportional mortality from autoimmune diseases was higher (2.3% vs 1.7%) for teachers than for decedents in other professional occupations (Table 1). Elevated proportional mortality held for male teachers, for teachers in both racial groups, and for teachers in every age group. Unadjusted proportional mortality was essentially equal for female teachers and for females in other professions (2.4%). In contrast to the trend observed among teachers, proportional mortality from autoimmune diseases among other professionals was relatively constant across the 25–84 age range.

Standardized proportional mortality ratios. Elevated proportional mortality from autoimmune diseases among teachers persisted after adjustment for potential confounding factors (Table 2). Statistically significant, standardized PMR exceeded 100 for all teachers, for teachers of both sexes, and for teachers in both racial groups. Standardized PMR were also significantly inflated in every age group in the 35–84 range. The largest PMR (149) occurred in the 35–44 age interval. PMR consistently declined across all older age groups. By the over-85 age interval, the PMR for teachers versus other professionals

Table 2. Standardized proportional mortality ratios (PMR) comparing the frequency of autoimmune disease deaths among school teachers to that among other professional occupations.

	PMR*	95% CI	p
All teachers	113	(109,117)	< 0.0001
By sex			
Men	124	(112, 136)	< 0.0001
Women	111	(107, 116)	< 0.0001
By race			
White	112	(108, 117)	< 0.0001
Non-White	118	(105, 131)	0.005
By age			
25–34	102	(68, 148)	0.96
35–44	149	(126, 174)	< 0.0001
45–54	144	(126, 164)	< 0.0001
55–64	127	(113, 142)	< 0.0001
65–74	118	(108, 128)	0.0002
75–84	108	(102, 114)	0.01
≥ 85	102	(95, 109)	0.56

*Expressed in percentages and reflect standardization for age, sex, and/or race as appropriate relative to stratification.

Table 1. Deaths from all causes and from autoimmune diseases among teachers and persons in other professional occupations, United States, 1985–95.

	School Teachers		Other Professionals	
	Deaths From All Causes	Deaths From Autoimmune Diseases (%)	Deaths From All Causes	Deaths From Autoimmune Diseases (%)
Total	143,553	3259 (2.3)	717,095	11,988 (1.7)
By sex				
Men	25,740	419 (1.6)	482,662	6380 (1.3)
Women	117,813	2840 (2.4)	234,433	5608 (2.4)
By race				
White	131,133	2942 (2.2)	673,356	11,138 (1.7)
Non-White	12,420	317 (2.6)	43,739	850 (1.9)
By age				
25–34	1122	28 (2.5)	15,522	264 (1.7)
35–44	3753	154 (4.1)	32,259	619 (1.9)
45–54	6224	225 (3.6)	51,288	908 (1.8)
55–64	10,516	314 (3.0)	100,730	1770 (1.8)
65–74	19,174	569 (3.0)	177,527	3264 (1.8)
75–84	44,926	1154 (2.6)	205,587	3584 (1.7)
≥ 85	57,838	815 (1.4)	134,182	1579 (1.2)

(102) was virtually equal to the null value of 100. The trend in PMR relative to age was statistically significant ($p < 0.0001$).

Mortality from specific autoimmune diseases. When teachers were compared to other professionals on a disease-by-disease basis, PMR greater than 100 resulted for 11 of the 13 autoimmune diseases (Table 3). However, only 4 of these PMR were statistically significant — those for multiple sclerosis, RA, SS, and SLE. The greatest relative excess in autoimmune disease mortality among teachers occurred for multiple sclerosis (PMR = 161). Although multiple sclerosis was present in only 12.0% of autoimmune disease deaths among teachers, it accounted for 39.9% of the observed total excess (371.6 cases) in autoimmune disease deaths. PMR were greater than 100 for each of the rheumatic diseases and a significant PMR of 110 was observed for the rheumatic diseases in aggregate. A rheumatic disease was cited in 67.3% of the autoimmune disease deaths among teachers. Excess occurrence of rheumatic diseases accounted for 53.1% of the total excess in autoimmune disease mortality. PMR did not reach statistical significance for autoimmune diseases other than multiple sclerosis and the rheumatic diseases. The nonsignificant excess in mortality from these other autoimmune diseases accounted for only 7.0% of the total excess despite the fact that these diseases were cited in 21.3% of all autoimmune disease deaths among teachers.

Age trends for specific diseases. The trend in PMR relative to age that occurred among teachers for all 13 autoimmune diseases was replicated for the rheumatic diseases (Figure 1). The trend was statistically significant ($p < 0.0001$) as were individual PMR in the 35–44, 45–54, 55–64, and 65–74 age intervals. Among the rheumatic diseases, statisti-

cally significant trends (Table 3) based on higher mortality in younger age groups and lower mortality in older groups held for rheumatic fever and heart disease and for SLE. Across the 7 age categories (from youngest to oldest) the age-specific PMR for rheumatic fever were 127, 162, 145, 119, 113, 102, and 87, and for lupus were 112, 152, 169, 114, 97, 87, and 127. For multiple sclerosis, PMR were greater than 100 in all but the youngest age group and each PMR in the 35–84 age range was statistically significant. However, the trend in PMR relative to age was not statistically significant ($p = 0.15$). Instead, mortality was most elevated in the 45–54 age group and systematically declined across both younger and older groups. For the other autoimmune diseases, a PMR of 146 ($p = 0.04$) occurred in the 35–44 interval; PMR were close to 100 in all other age intervals and the trend test was not significant ($p = 0.82$).

Mortality among young and middle aged teachers. Although the significant inverse trend in excess mortality relative to age held only for 2 specific diseases, evidence of elevated mortality among young and middle aged teachers occurred across the autoimmune diseases. In the 35–44 age interval, PMR were greater than 100 for 11 of the 13 autoimmune diseases (data not shown). The 2 exceptions (Graves' disease and SS) were both instances in which no deaths among teachers occurred in that age group. For 5 diseases, PMR in the 35–44 age group were the largest across all 7 age groups: autoimmune hemolytic anemia (PMR = 277), glomerulonephritis (161), myocarditis (134), polymyositis/dermatomyositis (172), and rheumatic fever and heart disease (162). In the 45–54 age interval, PMR were greater than 100 for 9 of the 13 diseases. For 5 diseases, PMR were more inflated in the 45–54 interval than in any other interval: Addison's disease (PMR = 175), multiple sclerosis

Table 3. Proportional mortality ratios for deaths from specific autoimmune diseases among school teachers versus persons in other professional occupations.

	Observed Deaths	PMR*	95% CI	PMR p	Age Trend p
Multiple sclerosis	391	161	146, 178	<0.0001	0.15
Rheumatic diseases	2194	110	105, 115	<0.0001	<0.0001
Polymyositis/dermatomyositis	60	108	83, 140	0.57	0.98
Rheumatic fever/heart disease	784	104	97, 112	0.27	<0.0001
RA	996	112	105, 119	0.0005	0.07
Scleroderma	147	117	99, 137	0.07	0.71
SS	36	148	104, 205	0.03	0.50
SLE	197	117	101, 134	0.04	0.03
Other autoimmune diseases	695	104	96, 112	0.32	0.82
Addison's disease	82	109	87, 136	0.45	0.32
Autoimmune hemolytic anemia	20	87	53, 135	0.63	0.24
Glomerulonephritis	390	103	93, 113	0.62	0.80
Graves' disease	11	76	38, 136	0.45	0.21
Myasthenia gravis	77	110	87, 138	0.42	0.96
Myocarditis	115	107	89, 129	0.48	0.33

*Expressed in percentages and adjusted for age, sex, and race.

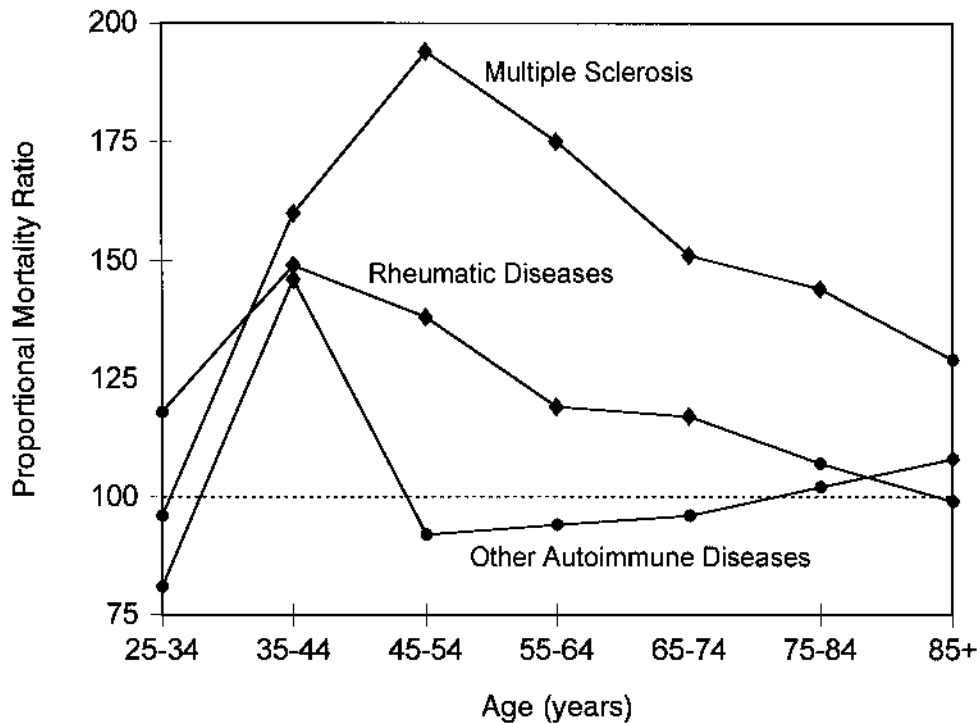


Figure 1. Trends in age-specific proportional mortality ratios (PMR) for 3 groups of autoimmune diseases among school teachers. Broken line: nominal value of 100; ◆: PMR that were statistically significant; ●: PMR that were not significant.

(194), myasthenia gravis (225), SS (260), and systemic lupus erythematosus (169).

Comparison of elementary and secondary teachers. When teacher decedents were stratified based on employment in elementary or secondary schools, the observed associations with autoimmune disease mortality remained. The results for elementary teachers replicated those for all teachers and are not shown. This was not surprising, in that elementary teachers made up more than 89% of the sample of teacher decedents. Results for secondary teachers showed uniformly stronger effects of teaching on autoimmune disease mortality than observed for all teachers or for elementary teachers alone (Table 4). The accentuation of the effect was sufficiently strong that autoimmune disease mortality among secondary teachers was significantly greater than that among elementary teachers in total, in women, in whites, and in the 35–44 age group. The PMR for secondary teachers in the 35–44 age interval was 243 ($p < 0.0001$) in comparison to other professionals, and was 155 ($p = 0.03$) in comparison to elementary teachers. In this age group, significant PMR for secondary teachers relative to other professionals occurred for multiple sclerosis (305, $p = 0.002$) and SLE (282, $p = 0.04$).

Analyses restricted to the 1989–95 period. Results for the 1989–95 period were the same as for the 1985–95 period. The standardized PMR for total autoimmune disease

mortality among teachers versus decedents in other professional occupations was 115 ($p < 0.0001$). Significantly elevated PMR occurred for male teachers (PMR = 131, $p < 0.0001$), female teachers (PMR = 113, $p < 0.0001$), white teachers (PMR = 115, $p < 0.0001$), non-white teachers (PMR = 119, $p = 0.01$), and in every age group in the 35–84 range. There was a significant trend in excess mortality relative to age ($p < 0.0001$), with PMR of 153, 145, 129, 125, and 112 in the 35–44, 45–54, 55–64, 65–74, and 75–84 age groups, respectively. Mortality was elevated for both elementary (PMR = 113, $p < 0.0001$) and secondary teachers (PMR = 138, $p < 0.0001$).

DISCUSSION

The NIOSH survey of occupational mortality unexpectedly pointed to elevated autoimmune disease mortality among school teachers during the 1984–88 period. Our results show that significant elevated mortality also occurred in the subsequent 1989–95 period. Thus, it is unlikely that the findings of the NIOSH survey only reflect repeated statistical testing. In our study we combined data from an 11 year period between 1985 and 1995. Accordingly, we were able to provide more detailed analyses concerning the characteristics of teachers affected by autoimmune diseases and the specific diseases involved. We restricted the control population to decedents in other professional occupations and so

Table 4. Proportional mortality ratios (PMR) for autoimmune diseases among secondary school teachers in comparison to other professional occupations and elementary school teachers.

	Observed	vs Other Professional Occupations			vs Elementary School Teachers		
		PMR*	95% CI	p	PMR*	95% CI	p
All secondary teachers	365	130	117, 144	< 0.0001	112	101, 124	0.04
By sex							
Men	92	128	104, 158	0.02	103	83, 126	0.82
Women	273	130	115, 146	< 0.0001	115	102, 130	0.02
By race							
White	339	129	116, 144	< 0.0001	112	100.2, 124	0.047
Non-white	26	138	90, 202	0.14	114	75, 167	0.55
By age							
25–34	0	0	0, 88	0.03	0	0, 85	0.03
35–44	31	243	165, 344	< 0.0001	155	106, 220	0.03
45–54	31	153	104, 217	0.03	104	71, 148	0.88
55–64	42	135	97, 182	0.07	105	76, 142	0.78
65–74	67	124	96, 157	0.10	107	83, 136	0.61
75–84	122	129	107, 154	0.007	119	99, 142	0.07
≥ 85	72	110	86, 139	0.45	106	83, 134	0.63

*Expressed as percentages and reflect standardization for age, sex, and/or race as appropriate relative to stratification.

limited the likelihood of confounding by socioeconomic status. We identified autoimmune disease deaths by reference to both underlying and contributing causes cited on death certificates. This increased the number of autoimmune disease deaths identified. It also increased the likelihood that reported PMR approximate standardized mortality ratios and so represent the true effects of teaching on risk of mortality from autoimmune diseases.

The dominant model of pathogenesis of the autoimmune diseases maintains that autoimmunity occurs when a genetically susceptible host encounters an appropriate environmental trigger²². If this model is correct, then among every cohort of new teachers there are those who are genetically predisposed to autoimmunity. If an environmental factor associated with teaching is sufficient to trigger an autoimmune response, then susceptible individuals will, in the time following their entry into the teaching profession, develop autoimmunity, become symptomatic, be diagnosed, and die from their disease in disproportionate numbers relative to susceptible individuals who enter other occupations.

Among teachers, the trends in autoimmune disease mortality relative to age are consistent with this model. The strongest effect of teaching on total mortality was observed in the 35–44 age interval. There was no evidence of excess mortality in the 25–34 interval. Excess total mortality steadily declined after age 45. Thus, on the one hand, the evidence points to the absence of a cumulative effect of teaching on autoimmune disease mortality. This is consistent with the depletion of susceptible individuals over time. On the other hand, the findings point to a 15 to 20 year period between the initial time of teaching (usually at age 21 or 22) and the first time of increased risk of death from

autoimmune diseases (at or after age 35). Relative to age, the timing of this period coincides with the typical patterns of pathogenesis and clinical course for autoimmune diseases like multiple sclerosis and SLE. Yet for some reason, among teachers the amount of autoimmune disease mortality in this period is amplified. If the amplification reflects increased incidence relative to other occupations, then the results suggest exposure to an occupational risk factor relatively early in teachers' careers.

Death certificates provide no information about specific exposures that any decedent actually experienced. Therefore, the association between teaching and autoimmune disease mortality provides merely a basis for speculation regarding exposures encountered by teachers and their effects on risk of autoimmune disease. Perhaps the most reasonable exposure factor to suspect is one or more infectious agents. The role of schools in the spread of influenza, varicella, Epstein-Barr virus, rhinoviruses, and streptococcal infections is well established^{23,24}.

Infections have long been suspected as risk factors for the autoimmune diseases²⁵. This is most clearly the case for rheumatic fever, in which an association with prior infection by Group A streptococcal bacteria is known, but incompletely understood²⁶. Among teachers, the pattern of excess mortality from rheumatic fever followed that for all autoimmune diseases, with the greatest elevation occurring in the 35–44 age group. Considering the rarity of rheumatic fever in the US during the 1985–95 period, this finding is surprising. However, it is consistent with reports of “outbreaks” of rheumatic fever in “low risk” groups of children and young adults across the US in the late 1980s²⁷.

Epstein-Barr virus is suspected to have a role in the

pathogenesis of a number of autoimmune diseases including autoimmune hemolytic anemia, multiple sclerosis, RA, SS, and SLE²⁸⁻³¹. Infectious mononucleosis, the clinical expression of acute Epstein-Barr infection, is one of the few infectious diseases strongly associated with secondary school students³². Notably, in our study, autoimmune disease mortality was most strongly elevated among secondary school teachers. In particular, significant excess mortality from multiple sclerosis and SLE occurred in the 35–44 age interval of secondary teachers. One study reports that delayed development of childhood infections is a risk factor for multiple sclerosis³³. Infection with Epstein-Barr virus in the US typically occurs in teenagers and young adults. This is later than in economically less developed countries in which infection usually occurs in young children and rarely leads to symptoms deserving clinical attention³². In the US, young adults who have not experienced Epstein-Barr infection before the time they begin their teaching careers may face greater risk of developing infectious mononucleosis and could be at higher risk of an autoimmune response to that infection.

If one assumes that occupations that involve prolonged, close contact with large numbers of people create greater opportunities for transmission of infectious agents, then the NIOSH survey points to occupations, other than school teaching, that provide additional support for the infectious trigger hypothesis of autoimmune pathogenesis^{7,9}. The survey found statistically significant excess mortality from multiple sclerosis in at least one sex and race combination for armed forces personnel, hairdressers, nurses' aides, post-secondary teachers, and students. Aggregation of data for white males and females also pointed to increased multiple sclerosis mortality among physicians. For rheumatic fever, mortality was significantly greater than expected among white male post-secondary teachers. Mortality from musculoskeletal diseases (including connective tissue diseases and RA) was significantly elevated in at least one sex and race combination for elevator operators, hairdressers, health technicians, nurses' aides, and social workers. Despite these findings, it is important to note that, in the NIOSH survey, most occupations with significantly elevated mortality in any autoimmune disease category were not ones obviously associated with greater potential for infectious disease exposure. While this does not refute the possibility that infectious agents trigger autoimmunity, it does appear to imply that infectious agents do not provide the only triggers.

For the autoimmune diseases, mortality, as assessed from death certificates, offers only a distant view of the circumstances that preceded incidence. Rarely is autoimmune disease diagnosis followed quickly by death. By the time of death, a person's prediagnosis occupation may no longer be their "usual occupation." For most cases, the chronic nature of their autoimmune disease provides ample opportunity for other conditions, related to autoimmunity or not, to domi-

nate the processes that lead to death and to be cited as the cause of death. Because of this, issues related to misclassification bias are of particular concern in judging the validity of our findings.

A number of studies document the frequency of misclassification of the occupations and causes of death cited on death certificates³⁴⁻³⁷. If such misclassifications usually occur at random, their primary effect should be to weaken estimates of real associations between occupation and disease, i.e., nondifferential misclassification bias³⁸. That we found consistent associations between teaching and autoimmune diseases implies that the degree of nondifferential misclassification bias was not sufficient to obscure these associations. However, there is also the possibility that school teachers are distinct from other occupations in regard to education, income, and interaction with the health care system, and, consequently, the accuracy or detail with which their death certificates are completed. Any mechanism by which teachers with autoimmune diseases are more likely than persons in other occupations to have those conditions cited on a death certificate would lead to artificially inflated measures of association, i.e., differential misclassification bias³⁸.

We attempted to reduce the potential for differential misclassification bias by using a control group based on other professional occupations. It seems reasonable to expect that similar socioeconomic status leads to similar patterns of death certificate accuracy. Yet reduction of the potential for bias does not imply its elimination. There is evidence that many nonprofessional decedents are "promoted" into professional occupations when their death certificates are completed³⁴. Among the teacher decedents in our study, this was probably not a serious problem, in that only individuals who were specifically identified as either elementary or secondary teachers were included. The professional credentials for elementary and secondary school teachers are well established and relatively uniform across the nation. Misclassification of decedents as professionals probably posed a more serious problem in the control group, i.e., the non-teacher professionals. If nonprofessional decedents are less likely than professionals to have existing autoimmune diseases cited among their causes of death and if their occupations are frequently misrepresented as professional occupations on death certificates, then the reported associations between teaching and autoimmune disease mortality may be exaggerated. Partly in anticipation of this problem, we performed another comparison: we compared secondary teachers to elementary teachers. The elevation in autoimmune disease mortality among secondary teachers was of such magnitude that the key associations persisted despite the change in control groups. In terms of socioeconomic status, elementary teachers probably constitute the ideal comparison group for secondary teachers.

Recently, epidemiologists have begun to study autoimmune diseases as a group that, in aggregate, may yield more information about etiologic pathways than has resulted from studies of individual diseases^{17,39,40}. A workshop organized by the US National Institute of Environmental Health Sciences concluded by emphasizing the need to determine common aspects of pathogenesis among the autoimmune diseases and, by doing so, to identify shared risk factors⁴¹. Our study contributes to that effort by identifying an occupation that experiences elevated autoimmune disease mortality and that offers the possibility of conducting observational studies of environmental exposures that alter risk of the autoimmune diseases.

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