An Investigation into a Potential Relationship between the Rise in Lanthanide Usage and the Increased Prevalence of Childhood Asthma

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Science

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Abstract

Asthma prevalence and mortality have been increasing in the United States over the last few decades. A particular increase in childhood asthma prevalence as estimated by hospital discharge rates has been noted. During the time period in which asthma prevalence and mortality have been increasing, the national usage of lanthanides have also been on the rise. An investigation into whether an increased exposure to lanthanides is one of the causes of the increased levels of asthma, particulary in children, has begun. This relationship can be tested by establishing whether local trends in childhood asthma correlate with local levels of exposure to lanthanides as measured in human and/or environmental media. Epidemiological analyses of public health records, historical research into levels of lanthanide usage and emissions, and experimental studies of environmental exposures, have all been conducted in order to attempt to establish whether such a relationship exists. These studies have been limited, however, by the lack of historical records of asthma prevalence, as well by the lack of local estimates of lanthanide exposure, available for analysis. It appears that lanthanide emissions may be related to increased asthma rates in a small and non-specific manner, at least in the Northeast United States. However, elevated concentrations of lanthanides have not been detected in children's hair in Woburn, MA, and evidence for a specific role of lanthanides in the observed increase in asthma prevalence remains unclear.

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An Investigation into a Potential Relationship between the Rise in Lanthanide Usage and the Increased Prevalence of Childhood Asthma

Chapter 1: Introduction

Asthma can be defined as a chronic airway inflammatory disorder which causes multiple respiratory symptoms such as bronchoconstriction, recurrent airflow limitation, and airway hyperresponsiveness. Symptoms of this respiratory disorder can include wheezing, lack of breath, coughing and tightness of chest. Multiple factors can be associated with the onset of asthma, including a genetic predisposition to the disorder, referred to as atopy.[1] Concern about asthma has recently risen due to the increasing prevalence of the disorder, particularly amongst children. The specific causes for this rise in asthma have yet to be isolated.

During the time period in which asthma prevalence and mortality have been increasing, the national usage of lanthanides have also been on the rise. Lanthanides are rare earth elements used in various industries including petroleum refineries and motor vehicle catalytic converters. This thesis explores available evidence to discover if there is a causal relationship between this increase in lanthanide emissions and the rise in asthma prevalence. Associations between asthma and various other metals in occupational settings, such as platinum, cobalt, nickel, chromium and aluminum, have been documented,[2] and suggest that such an association between lanthanides and asthma is pathologically feasible.

An investigation into whether an increased exposure to lanthanides is one of the causes of the increased levels of asthma, particularly in children, in the United States has begun. This relationship can be tested by establishing whether local trends in childhood asthma correlate with local levels of exposure to lanthanides as measured in human and/or environmental media. Asthma rates and lanthanide exposures should be compared over three major time periods of interest: pre-1965, during which time there were no known anthropogenic sources of lanthanides; 1965 - 1980, during which time lanthanides were used in cracking processes in petroleum refineries; and 1981 - present, during which time lanthanides have been used in motor vehicle catalytic converters in addition to in refineries.

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[1] .....Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention NHLBI/WHO Workshop Report (Based on a March 1993 Meeting). National Institutes of Health, Publication Number 95-3659, January 1995.

[2] .....Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention NHLBI/WHO Workshop Report (Based on a March 1993 Meeting). National Institutes of Health, Publication Number 95-3659, January 1995.

Hence, epidemiological analyses of public health records, historical research into levels of lanthanide usage and emissions, and experimental studies of environmental exposure, have all been conducted in order to attempt to establish whether a relationship exists between lanthanide emissions and childhood asthma. These studies were limited, however, due to the lack of historical measures of local area asthma prevalence, as well as of regional levels of lanthanide exposures, available for analysis.

Chapter 2: Asthma Epidemiology

Estimations of asthma prevalence amongst Americans range from 12 - 14.6 million people, of whom 4.8 -5 million are estimated to be children. In addition, at least 5000 Americans a year are estimated to die due to this disorder.[3,4] An increase in the mortality due to asthma and, to some extent, in the overall prevalence of asthma, has been witnessed in the United States over the last few decades, despite a decrease in mortality rate between 1950 - 1978[5]. Data from the National Hospital Discharge Survey (NHDS, discussed below) show a greater than 200% increase for children and an approximately 50% increase for adults in asthma hospitalization rates between 1965 - 1983[6]. Asthma hospitalization rates have continued to increase into the 1990s. In order to fully understand the epidemiology of asthma in both children and adults, local area estimates of prevalence need to be analyzed. Ideally, small area estimates of childhood asthma prevalence dating back to the early 1960s need to be obtained. However, such historical records do not exist, and there are tremendous limitations in obtaining any asthma prevalence statistics dating prior to the mid-1980s. An investigation into the available sources of public health records must first be conducted, in order to discover possible sources of data on local area asthma prevalence. Some particularly helpful and informative individuals whom can be contacted when searching for such data are listed in Appendix A.

2.1 *Sources of Statistical Records of Asthma Prevalence and Mortality*

Epidemiological records of most diseases can be thought of in terms of either prevalence and incidence, which reflect how many people have a particular disorder, or in terms of mortality, which describes how many deaths have occured due to a particular ailment. One of the largest

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[3] American College of Allergy, Asthma and Immunology. Asthma Facts. Arlington Heights, IL. January 1997. Fax received April 23, 1997.

[4] Cowley, GC and Underwood, A. The Scary Spread of Asthma and How to Protect your Kids: Why Ebonie Can't Breathe. Newsweek. May 26, 1997, 58 - 64.

[5] Sly, Michael R. Increases in Deaths from Asthma. Annals of Allergy. 53, July 1984, 20 - 25.

[6] Evans, III, R, Mullally, DI, Wilson, RW, Gergen, PJ, Rosenberg, HM, Grauman, JS, Chevarley, FM, and Feinleib, M. National Trends in the Morbidity and Mortality of Asthma in the US: Prevalence, Hospitalization and Death from Asthma over Two Decades: 1965 - 1984. Chest June 1987; 91: 6: 65S - 74S.

problems to overcome in tracing the epidemiology of asthma are the drastic changes which have occurred in the accepted definition and diagnosis of the disorder. For example, a redefinition of asthma occurred in the 1970s. Even if archival records for asthma could be obtained, drastic classification changes could lend inaccuracy to longitudinal comparisons of rates of the disorder, particularly if hospital discharge statistics are being used. It is very difficult to account for such classification changes as well as for the variability in physician diagnoses and in recording patterns.[7,8] The lack of proper records of the history of asthma prevalence is recognized as a major obstacle and source of frustration for many epidemiologists, and was the largest single problem encountered in this work.

2.1.1 Prevalence of Asthma

In order to compare the prevalence of asthma in different geographical regions, prevalence rates need to be generated based on estimated prevalence and population statistics for a given area. Unfortunately, sources of asthma prevalence statistics are very limited. Measures of both adult and childhood asthma prevalence can be found on a national level, since the National Center for Health Statistics conducts various health surveys which provide national estimates of asthma prevalence. One such survey is the National Health Interview Survey (NHIS), conducted by the National Center for Health Statistics. Data is collected via a house to house sampling around the nation and includes questions regarding asthma beginning in 1970. For children, information gathered could have been self-reported or reported by proxy. Various sources of sampling error, such as non-responses and over/undersampling of particular ethnic or age groups, are inherent in such a survey. Sampling weights are used in generating national estimates in order to attempt to account for such sampling biases. However, changes in survey questionnaires and in physician diagnoses patterns are still possible sources of error when comparing data over several decades. Unfortunately, due to the sampling design employed by the survey, the data collected cannot be used to calculate accurate estimates at the state or county level, as is discussed below.[9,10]

The National Health and Nutrition Examination Surveys (NHANES), also conducted by the National Center for Health Statistics, also reports national estimates of disease prevalences. However, this data was not gathered for any particular age group for a large number of years

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[7] Utell, Mark. University of Rochester. Telephone conversation, June 27,1996.
[8] Aschengrau, Ann. Boston University School of Public Health. Telephone conversation, Boston, MA. 1996.
[9] Evans, III, et al., 1987.
[10] Horm, John W. National Center for Health Statististics. Hyattsville, MD. Personal Communication. August 9, 1996.

consistently. A few state departments of health collect statistics on asthma prevalence, though most states have not labeled asthma as a reportable disease and as such do not track prevalence of the disorder. Those states which do have prevalence estimates generally have not calculated it for many years, nor do they necessarily report estimates for local areas within the states. The American Lung Association has calculated local area prevalence estimates, based on NHIS statistics. Prevalence rates, however, cannot be calculated from these estimates, as will be discussed below. Thus the only direct estimates of asthma prevalence from which rates can be obtained are national, and even these do not provide data regarding asthma prevalence in the 1960s.[11]

Somewhat more detailed statistics of hospitalizations due to asthma are available at both the national and state levels. Asthma hospitalization data usually consists of the number of inpatient discharges for patients diagnosed with asthma, per year, for a given area. Though hospital discharge data can be used as a rough estimate of prevalence, two main sources of error are associated with this extrapolation. First, a large number of people with asthma are never hospitalized for the condition, due to a lack of severity, due to effective treatment in an emergency room alone, or, especially in more urban or impoverished areas, due to negligence or lack of available resources. Furthermore, physicians may fail to diagnose asthma in some patients who do reach hospitals, since asthma can be difficult to distinguish from other respiratory diseases. The nature of clinical symptoms associated with asthma adds to this diagnostic difficulty. Many asthmatic symptoms, such as bronchospasm, vary in extent and remain quiescent for long periods of time, such that physicians could overlook the disorder in temporarily asymptomatic patients. Thus, hospital discharge data may give low estimates of prevalence, and may be more representative of trends in severity or in poor treatment rather than in occurrence. Cumulative discharge data, the average or sum of discharges over multiple years, may account for diagnoses missed during first hospitalizations, and as such may provide more accurate estimates of prevalence. [12,13,14,15] The second source of error, on the other hand, as emphasized by Bob Pokras[16] of the National Center for Health Statistics, and Ann Aschengrau[17] of the Boston University School of Public Health, occurs since hospitalization rates do not

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[11] Evans, III, et al., 1987.
[12] Kurt Maurer, National Health and Nutrion Examination Surveys/National Heatlh Examination Surveys, National Center for Health Statistics, telephonic communication, Hyattsville, Maryland, April 9,1997.
[13] Evans, III, et. al., 1987.
[14].....Global Initiative for Asthma 1995.
[15] Weiss, Kevin. Rush Institute for Primary Care. Center for Health Services Research. Telephone conversation, June 2, 1996.
[16] Pokras, Bob. National Center for Health Statistics, telephone conversation, Hyattsville, Maryland, April 9,1997.
[17] Ann Aschengrau, Boston University School of Public Health, telephone conversation, Boston, Massachusetts, 1996.

account for multiple visits by one patient in a given year. Thus hospital discharge data may overestimate prevalence, due to this duplication.

As is obvious from the above discussion, comparisons of hospital discharge rates from one county or region to another must be done with caution, due to the multitude of confounding factors which may influence calculated statistics. Nevertheless, hospitalization data does provide some estimate of relative rates of asthma in a given area, and is one of the only available sources of historical records relating to asthma. As such, hospital discharge rates are heavily relied upon in this research.

The National Hospital Discharge Survey (NHDS), also conducted by the National Center for Health Statistics, is a recurrent survey in which information on nonfederal, short-stay hospital discharges by diagnoses is collected. This survey provides both national and regional estimates of hospitalizations due to asthma dating to approximately 1965, and is an important source of information on asthma prevalence, excepting a few caveats, such as sampling biases.[18]

Many state departments of health or local private agencies also maintain records of inpatient admissions or discharges by diagnoses, and are able to provide numbers of patients hospitalized for asthma by select age groups and by county or zip code. Such data was obtained and analyzed for New York State from the state Department of Health. Though these records extend into the mid 1980s and were available at no cost, most state records only cover even more recent years, and many require a processing fee to be paid in order to generate the data by age and local area groups. Though this data does not provide the longitudinal picture ideal for our research, it can pinpoint local areas currently suffering from high rates of asthma prevalence. Differences in data collection methods and purposes may lead to biases when comparing hospital discharge data from multiple states, especially since some sources of such data are private for-profit agencies.

Many of the states which have been contacted in an attempt to obtain hospital discharge records are shown in Table 1 below. The time period over which states have discharge data over small regions such as zip code, county or hospital service area are also shown for most states. Where applicable, fees vary and are usually based upon the time necessary for data extraction, and most would probably range from 100 - 500 dollars.

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[18] Graves, EJ 1993 Summary: National Hospital Discharge Survey. Advance Data from Vital and Health Statistics. No 264. Hyattsville, Maryland: National Center for Health Statistics. 1995.

Table 1: State Sources of Hospital Discharge Data

State	Time Period, if any, over which Asthma Discharge Data Available	Source and Cost	Contact Person and/or Telephone Number
Alabama	none		DOH, (334) 206-5347
Alaska	outpatient 5/92 - 5/94	Gordian Paper, 1997	
California	1990 - 1995	DOHS Chronic Disease Control*	Kay Dewitt, (916) 323-3686
Colorado	1988 - 1995, ?1996	Colorado Hospital Association, Fee	Bob Fynn, (303) 758-0047
Connecticut	1991 - FY 1996	Connecticut Office of Health Care Access	David Walker, (860) 418-7040
Delaware	1992 - 1995	Deparment of Health and Social Services: Health Planning	Ted Jarrell, (302) 739-4776
Florida		Agency of Health Care Administration	Doug Cook, (904) 922-3809
Hawaii	1988, 1993 prev	DOH Preventive Health Services Branch	Judy Mikami, (808) 587-3900
Ohio	1987/88 - 1995	Health Care Data Center, Fee	Bill Ramsin/Jon Paulson, (614) 644-8507
Maryland		St. Paul's Hospital, Fee	Richard Benson, (410) 760-3447
Massachusetts	1978 - 1996; 1986 -	Massachusetts Health Data Consortium, Fee; DOPH	Richarch Senicola (617) 890-6040; Bill Allan, (617) 451-5340, x397
Michigan	1980s - 1990s	DOPH	Stan Nash, (517) 335-8045
Missouri	1993 - 1995	DOH, Center for Health Statistics	Barbara Hoskins, (573) 751-6279
New Hampshire	1986 - 1995	Department of Health and Human Services, Possible Fee	Ken Ruth, (603) 271-4671
New Jersey	1986 - 1995	DOH	Jon Polito, (609) 292-9354
North Carolina	1989 - 1994; FY 1996	University of North Carolina: Sheps Center, Fee; HCIA, Fee	Virginia Estes, (919) 966-7112; LucieAnn Eyre, (919) 677-4125
North Dakota	1987 - 1995, 1/2 1996	Claims Data: DOH Health Information Systems Division	Gary Garland, (701) 328 - 2894
Oklahoma	1995	Health Care Authority	Matt Lucas, (405) 530 - 3439
Pennsylvania	1995	Health Care Cost Containment Council	Bob Maley, (717) 232-6787
Rhode Island		DOH Health Risk Assessment	Jay Buechner, (401) 277 - 2550
Vermont	1991 - 1995	DOH	Peggy Brozicevic, (802) 863-7280
Washington	1987/88 - 1995	DOH: Non-infectious	Juliet van Eenwyk,

		Disease Epidemiology	(360) 705-6051

*DOHS: Department of Health Services; DOPH: Department of Public Health; DOH: Department of Health

Investigations into asthma diagnosis or discharge records from individual hospitals have been conducted in some localized areas, such as in Washington, D.C.[19] In general, however, such investigations may not be fruitful in locating asthma records dating back more than 20 years, since many hospitals have not saved old patient records. If records prior to around 1980 are available, they are probably kept on paper, and searches through them would most likely prove to be very time consuming. Again, however, historical records may not reflect asthma trends with accuracy, due to drastic changes in the diagnosis and accepted definitions of asthma.[20,21] Furthermore, the ability to generate rates from these individual hospital derived statistics would be limited, since the total populations served by each hospital patient during each time frame would be uncertain. The ability to generalize statistics from a particular hospital or area to other areas or population groups would also be very limited due to differences in ethnic makeup, socioeconomic status, and health care quality.[22] Most importantly, access to hospital records is difficult to obtain due to patient confidentiality issues. Only if one is able to obtain clearance into hospital records where such data is kept, can records for individual areas be compiled and compared, unless someone within the hospital agrees to compile the information him/herself. However, though comparisons with or extrapolations to other communities would be limited, investigations into patient records of individual hospitals can be very valuable in studying trends within the community served by the hospital of interest. Unfortunately, the hospitals which are more likely to have saved older patient records are more likely to be located in very urban areas and/or in academic settings, neither of which are representative of the more general residential areas where effects of lanthanide emissions might more readily be observed.

Records from large insurance companies could provide another possible source of asthma statistics in the form of numbers of hospital discharges, office visits or other measures of health care utilization. Caution must be taken in using such data for epidemiological analyses, however, due to potential biases from specific characteristics of populations served by any particular insurance agency and due to specific motivations for data collection by these agencies, such as financial monitoring rather than tracking of public health.

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[19] Mullally, DI, Howard, WA, Hubbard, TJ, Grauman, JS, Cohen, SG. Increased Hospitalizations for Asthma among Children in the Washington, D.C. Area During 1961 - 1981. Annals of Allergy. 53, July 1984, 15 - 19.
[20] Mark Utell, University of Rochester School of Medicine, telephone communication, June 17 and 27, 1996.
[21] Aschengrau, 1996.
[22] Evans, III, et. al., 1987.

2.1.2 Mortality due to Asthma

Mortality rates, on the other hand, have been recognized as an important public health issue for the greater part of the century, and more detailed records of mortality than morbidity are available for asthma. Deaths due to asthma occur very seldomly. Since only 5000 deaths per year are estimated to be due to asthma, while up to 15 million people are estimated to have the disorder, it can be estimated that only approximately 0.03% of asthma cases result in death. These deaths are usually associated only with the most severe and/or the most poorly treated cases. Thus, while hospitalization rates are biased towards the population which is treated for asthma, mortality rates are biased towards that which receives negligible or even no treatment. Since asthma does not have a high risk of mortality, especially in children, the numbers of deaths due to asthma are generally very small, and not necessarily representative of asthma prevalence. Mortality data may be useful in looking at national or statewide trends,[23] in validating prevalence trends generated from other sources, or perhaps in evaluating relative severities of the disorder over studied time periods or amongst different ethnic groups in local areas. Many such studies have been conducted, such as Kaplan's analysis of asthma mortality rates in Pennsylvania[24] or Targonski et al.'s research on asthma mortality in Chicago.[25] However, such information is not likely to give accurate representations of local trends in asthma prevalence, or to provide prevalence rates which may be compared amongst different locations. Furthermore, physician classification and reporting of asthma as a cause of death has also undergone drastic changes since the 1960s, making comparisons across the decades less accurate[26].

The Vital and Health Statistics series from the National Center for Health Statistics publishes mortality data by county due to various causes, listing the "underlying cause" of death, and dates at least as far back as the early 1960s.[27]. However, records of deaths due to asthma alone are not available in the Vital and Health Statistics series. Rather, data for deaths due to bronchitis, emphysema and asthma (ICD codes 490 - 493, explained below) are available for 1968 - 1978, and data for deaths due to chronic obstructive pulmonary disease and allied conditions (ICD 490 - 496, including asthma) are available for 1979 - 1991. Thus, these records are not exclusive for asthma, and are discontinuous between 1978 and 1979. Furthermore, even

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[23] Sly, 1984.
[24] Kaplan, KM. Epidemiology of Deaths from Asthma in Pennsylvania, 1978 - 1987. Public Health Reports. 108: 1, January - February 1993, 67 - 69.
[25] Targonski, PV, Persky, VW, Orris, P, and Addington, W. Trends in Asthma Mortality among African Americans and Whites in Chicago, 1968 - 1991. American Journal of Public Health. 84 11, November 1994, 1830 - 1833.
[26] Evans, III, et. al., 1987.
[27] Evans, III, et. al., 1987.

the data within the 1979 - 1991 time period does not seem to give an accurate representation of asthma prevalence when compared to the estimate of prevalence obtained from hospital discharge rates, as can be seen in the comparison between mortality and hospitalization rates for New York State, as discussed below. Records of deaths due to asthma are available by county from many individual state Departments of Healths, and have been analyzed for the state of Minnesota.

2.2 Analysis of Asthma Statistics from Multiple Sources

2.2.1 National Levels of Asthma Prevalence

The following five estimates of national asthma prevalence have been derived from data collected by the NHDS and analyzed:

1) hospital discharge rates for children 0 - 14,
2) hospital discharge rates for adults 15 years of age and older,
3) total hospitalization rates, calculated by taking the sum of the above two estimates,
4) numbers of patients diagnosed with asthma as one but not necessarily the primary diagnosis (all listed diagnoses),
and
5) numbers of patients for whom asthma was listed as the primary diagnosis (first listed diagnosis).

Childhood and adult hospitalization rates were taken in part from NHDS data collected by Evans, III et al.[28] The 1985 childhood asthma rate was calculated using the 1985 population estimate from the World Health Organization. The National Center for Health Statistics separates diseases according to the Manual of the *International Classification of Diseases, Injuries, and Causes of Death (ICD)*. Classifications in the ICD have been adjusted over time, resulting in different editions being used during different time periods. With regards to the time periods of interest to us, the seventh edition was used between 1958 - 1967, the eighth between 1968 - 1978, and the ninth from 1979 to the present. In order to account for changes in this system of classification, numbers given under different ICD codings can only be compared after correction using comparability ratios. Thus, the National Hospital Discharge Survey ICD 8/ICD9 comparability ratio is 0.63, meaning that the ICD9 number is multiplied by 0.63 in order to make it comparable to the ICD8 data. Adjusting asthma data using comparability ratios is only accurate when done at the total population level, and thus is not meant to be done in order to analyze subgroups within the total population, such as race or age cohorts. However, having stated this, Evans, III et al.[29] use this comparability ratio to give adjusted values for such cohorts. Thus I

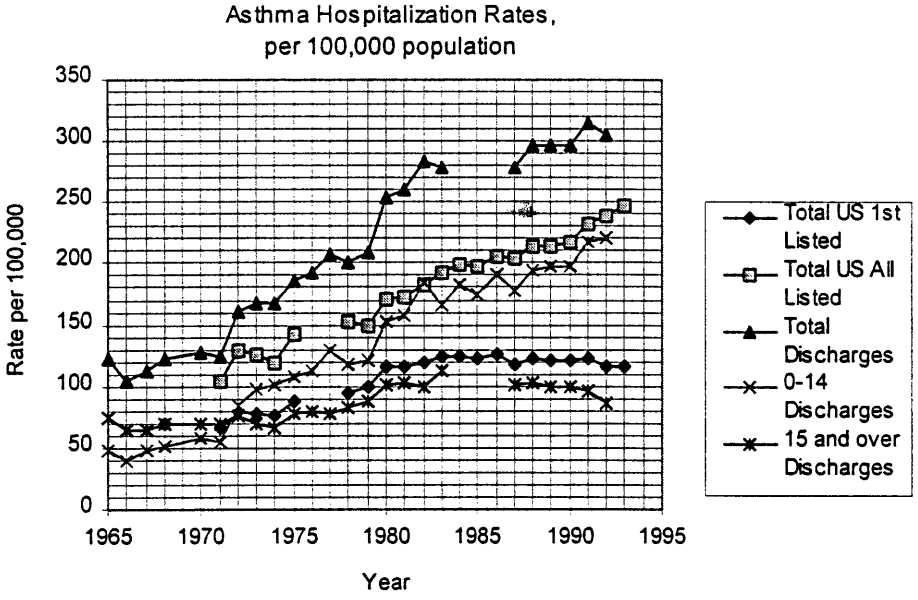
[28] Evans, III, et al., 1987.
[29] Evans, III, et. al., 1987.

have assumed that it is somewhat accepatable to use this correction factor in the analysis of population subgroups, accepting that the resulting values will contain some inherent errors. Again following the methods used by Evans, III et al., no corrections were performed when comparing data under ICD7 from that under ICD8. Differences between different ICD systems of classification not accounted for by the application of comparability ratios to subgroups provides one source of error in our estimate of prevalence trends based on hospitalization data. Furthermore, the change in ICD codes for asthma may reflect changes in accepted definitions of the disorder, or in criteria used in the diagnosis of asthma. These changes are not quantitatively accounted for, though they may have slightly contributed to increases observed in asthma rates.

As can be seen in the Figure 1 below, total hospitalization rates, childhood hospitalization rates, and total all listed asthma diagnoses all show a large increase, beginning in the 1970s and continuing into the 1990s. A linear fit to this data would give positive slopes of 8.4 for total hospitalizations, 7.0 for childhood hospitalizations, and 5.9 for total all listed diagnoses. On the other hand, total first listed diagnoses and adult hospitalization rates show a very slight increase in the 1970s, which levels off in the 1980s and 1990s. The slopes for adult hospitalizations would be 1.5, and that for total first listed diagnoses would be 2.4. Thus an increase can be observed in total hospitalizations due to asthma. This increase appears to largely be due to an increase in childhood hospitalizations, according to this data. First listed diagnosis rates serve as a subset of all listed rates. A rise in asthma prevalence is suggested by all listed diagnosis rates more than by first listed rates. Since these all listed rates are inclusive of patients whose primary ailment is not asthma, all listed diagnosis rates are probably better estimates of overall prevalence than first listed rates.[30]

[30] van Eenwyk, Juliet. Washington Department of Health, Noninfectious Disease Epidemiology. Telephonic Communication, April 1997.

Figure 1: National Asthma Discharge Rates from the NHDS



2.2.2 New York State Hospital Discharge Rates

New York State has a fairly advanced system of public health records. All counts of inpatient discharges diagnosed with asthma by county of patient residence for all patients 15 years of age or younger from 1984 - 1994 can easily be obtained from the Biometrics Division of the New York State Department of Health in Albany, New York. Though only data for years after 1985 can be taken with complete confidence, discharge rates from years after 1980 may be acccurate enough to use in locating counties of high asthma hospital discharge rates.[31] However, as stated above, only records of asthma hospitalizations dating from 1984 to 1994 are available. Like the data available for asthma hospitalizations from the National Center for Health Statistics, which classify all components of ICD-9 code 493 under asthma, we were able to obtain counts for all hospitalizations falling under all of the following ICD-9 codes:

493.00: extrinsic asthma without mention of status asthmaticus
493.01: extrinsic asthma with mention of status asthmaticus
493.10: intrinsic asthma without mention of status asthmaticus
493.11: intrinsic asthma with mention of status asthmaticus
493.20: chronic obstructive asthma without mention of status asthmaticus
493.21: chronic obstructive asthma with mention of status asthmaticus
493.90: asthma, unspecified, without mention of status asthmaticus
493.91: asthma, unspecified, with mention of status asthmaticus

[31] Utell, Mark. Telephone conversation, March 4, 1996.

As seen above, the ICD-9 classifies asthma into three main categories: a) extrinsic asthma, which is caused by environmental or external agents; b) intrinsic asthma, also known as essential asthma, in which no extrinsic agent can be detected,[32] and c) chronic obstructive asthma. A particularly persistent and severe asthmatic attack is referred to as status asthmaticus.[33] Due to the unknown nature of the clinical form under which asthma induced by lanthanides could mask, potential cases of asthma caused by lanthanides could have been categorized under any of the above categories. Thus the inclusive data set is more likely to show the effect, if any, of lanthanide emissions, and provides us with a more complete picture of total disability due to asthma.

The ten year data set of childhood hospital discharges due to asthma from 1984 - 1993 were retrieved by James H O'Meara, Biometrics Data Coordinator. A cursory look at all counts reveals that the number of cases falling under ICD-9 493.90 and 493.91 were often higher than those under other sub-categories. In order to calculate prevalence rates using this data, the total number of asthma cases for children under 16 was divided by the total under 16 population in each county for each year. Under 16 populations were estimated with the sum of live births in each county from the year of interest to 14 years prior to that year. Unfortunately, this estimate has many inaccuracies due to preferential migration of particular subgroups of the population in and out of certain counties, and due to under 16 deaths within counties. The estimate would not reflect large changes which often occur in county populations, and may have been too large an extrapolation to make.[34]

We now know that county estimates by 5 year age groups can be generated from Federal Census Bureau statistics obtained from Bob Scardamalia at the Empire State Data Collection Agency. These estimates could be manipulated to generate under 16 population estimates by using statewide age proportions to calculate the percent of 15 year olds accounting for the 15 - 19 year old population, and adding this population count to the data given for ages up to14. Estimates generated in this manner would have been more accurate than those generated using live birth statistics. A cursory look at 1993 5 year age group statistics suggests that estimates generated by live births are lower than those that would be generated by these 5 year estimates. Nevertheless, since estimates derived from live births were used consistently for all counties and

[32] International Dictionary of Medicine and Biology
[33] International Classification of Diseases. 9th Revision Clinical Modification (ICD-9-CM), 5th Edition. 1996.
[34] Horm, John W. National Center for Health Statististics. Hyattsville, MD. Personal Communication. August 9, 1996.

all years, the rates generated should still be comparable between different counties, though the absolute values of these rates may be too high.

The yearly and average childhood hospitalization rates between 1984 - 1993 for each county in New York State are shown in Table 2 below. Values are given per 10,000 people. New York City refers to the five city counties - Bronx, Kings, New York/Manhattan, Queens and Richmond - taken together. The data reveals 9 counties with hospitalization rates 50% above the state average of 35.3: Fulton (123.2), Montgomery (104.4), Bronx (97.8), New York/Manhattan (82.5), Kings (65.1), Hamilton (60.1), Cortland (59.0), Schuyler (56.9) and Genesee (54.9).

Table 2: New York State Asthma Discharges, Children under 16, by County, 1984 - 1993

County	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	Average
Albany	21.7	22.2	31.0	23.9	23.3	27.2	27.2	30.2	28.2	32.5	26.6
Allegheny	33.8	22.1	19.6	23.3	23.5	11.4	40.9	23.8	21.9	42.3	26.3
Broome	13.3	16.0	13.5	14.4	11.7	16.6	17.7	15.9	14.6	12.0	14.6
Cattaraug	41.8	38.8	54.9	48.2	36.7	36.2	52.5	37.3	36.8	35.1	41.8
Cayuga	28.2	76.0	52.1	31.0	24.0	22.1	16.8	20.0	20.5	25.4	30.6
Chautauqu	26.0	22.0	13.6	18.2	20.7	28.3	25.7	28.3	36.6	42.0	25.9
Chemung	14.7	13.1	18.2	22.6	19.2	18.2	22.1	25.5	25.1	28.5	20.8
Chenango	27.4	30.7	26.2	36.5	31.7	19.4	32.9	32.7	17.1	26.1	29.1
Clinton	11.9	11.9	19.7	15.0	11.9	13.9	17.3	21.9	27.4	27.5	17.8
Columbia	27.3	19.5	16.7	14.9	7.4	12.9	16.4	17.1	13.4	12.5	15.8
Cortland	93.7	92.7	118.7	72.0	27.4	31.3	35.0	32.9	47.2	38.6	59.0
Delaware	29.8	38.9	32.8	32.8	17.4	30.5	22.7	33.3	24.8	43.3	30.6
Dutchess	31.7	24.7	35.7	31.4	26.2	18.2	16.0	19.4	19.9	19.8	24.3
Erie	33.5	28.9	35.0	24.0	18.0	20.3	23.9	21.7	24.0	37.7	26.7
Essex	27.3	20.7	26.3	31.8	26.4	25.0	26.3	24.6	20.5	19.2	24.8
Franklin	43.1	21.8	37.0	26.4	51.3	35.5	25.7	31.0	22.4	21.5	31.6
Fulton	143.4	145.0	196.7	129.9	124.3	88.4	91.2	80.2	97.2	135.3	123.2
Genesee	68.3	54.5	57.6	71.8	57.1	48.6	67.1	28.9	52.7	42.3	54.9
Greene	20.5	16.3	17.7	19.1	17.7	14.9	10.8	7.9	14.3	12.9	15.2
Hamilton	150.9	43.7	55.4	88.7	22.5	34.6	68.9	56.7	56.5	22.9	60.1
Herkimer	25.7	22.4	23.5	18.4	24.5	24.6	26.3	17.3	36.6	36.1	25.5
Jefferson	63.8	60.0	67.0	47.7	38.0	35.1	43.8	36.8	37.6	28.6	45.8
Lewis	21.0	17.8	17.9	27.6	21.2	19.3	17.5	25.3	22.1	57.0	24.7
Livingsto	28.8	17.5	21.0	29.4	46.2	53.6	53.0	28.0	30.3	22.3	32.9
Madison	27.9	24.9	41.2	37.7	28.7	27.9	21.6	6.2	21.4	13.3	25.7
Monroe	20.3	18.0	25.1	21.6	22.7	21.0	29.9	23.3	24.5	26.1	23.3
Montgomer	117.4	123.3	173.0	99.7	87.2	84.4	90.3	105.4	76.9	85.9	104.4
Nassau	23.8	23.3	25.4	24.8	24.8	27.2	25.0	28.3	33.7	35.5	27.2
Niagara	76.4	63.6	56.8	49.1	45.1	36.5	42.3	34.7	46.2	46.0	49.7
Oneida	15.0	15.3	19.5	23.0	22.5	28.4	24.4	21.7	23.3	34.8	22.7
Onondaga	18.2	20.8	22.1	18.7	17.2	17.1	18.1	19.6	21.6	25.3	19.9
Ontario	17.7	16.7	23.9	23.3	17.6	8.2	17.7	15.3	9.8	11.2	16.1
Orange	53.6	50.4	50.5	46.0	48.2	48.4	45.0	45.8	34.3	32.3	45.4
Orleans	46.0	32.0	34.4	35.5	13.4	19.0	17.9	20.0	15.4	35.2	27.0
Oswego	31.3	29.2	41.9	32.1	22.2	25.7	24.4	23.8	28.6	27.5	28.7
Otsego	38.6	36.9	56.8	26.5	32.1	30.0	40.8	50.6	30.1	43.8	38.6
Putnam	30.5	42.5	50.4	30.0	25.4	22.7	21.0	29.0	32.5	35.7	32.0
Rensselae	19.9	19.6	19.9	21.8	11.8	14.7	23.7	29.6	20.4	34.2	21.6
Rockland	24.2	18.9	23.8	24.2	20.5	16.1	18.5	22.6	23.6	26.1	21.8
St. Lawre	49.2	38.6	37.7	36.8	24.8	25.4	18.7	32.8	27.7	36.1	32.8
Saratoga	35.8	28.4	42.8	35.6	27.3	28.1	45.4	41.1	34.3	42.3	36.0
Schenecta	18.3	16.3	26.1	23.7	24.1	27.7	33.9	38.8	30.8	42.1	28.2
Schoharie	18.1	5.4	16.6	11.0	24.1	3.7	15.0	26.1	25.7	25.5	17.1
Schuyler	93.4	41.4	68.1	102.2	83.7	23.6	23.6	54.7	47.1	31.5	56.9
Seneca	16.0	11.7	10.2	8.8	5.9	4.4	4.3	8.6	11.5	15.7	9.7
Steuben	54.1	33.5	35.7	38.0	42.8	51.4	46.7	40.2	37.2	36.5	41.6
Suffolk	28.3	26.0	27.7	27.6	27.0	28.8	29.5	31.7	28.5	25.3	28.0
Sullivan	28.6	28.2	17.6	32.8	25.8	26.8	21.6	33.3	27.0	42.7	28.3
Tioga	12.0	7.5	13.2	14.1	10.3	8.3	11.9	11.8	5.4	4.5	9.9
Tompkins	26.4	18.1	27.5	26.8	32.4	24.3	32.1	19.0	26.1	24.5	24.7
Ulster	24.4	26.5	26.1	17.3	19.8	17.8	17.5	19.1	17.7	23.5	21.0
Warren	48.7	32.4	48.5	26.0	40.8	42.5	50.2	41.9	31.3	31.3	39.4
Washingto	33.9	25.0	35.6	27.8	32.1	44.0	49.7	37.3	39.9	23.7	34.9
Wayne	38.6	32.8	42.7	31.7	27.7	22.0	30.5	23.9	18.9	21.6	29.0
Westchest	25.0	21.6	29.2	26.1	26.5	23.5	24.8	27.6	25.8	29.1	25.9
Wyoming	47.8	25.5	38.9	48.9	54.7	85.9	55.7	27.9	21.2	23.0	43.4
Yates	25.6	21.0	13.9	18.6	25.0	6.7	11.0	10.8	21.4	23.9	18.4
Bronx	88.4	73.7	80.3	74.0	79.4	84.8	97.4	112.8	137.4	149.4	97.8
Kings	61.5	61.3	62.0	61.8	54.4	60.1	63.5	67.9	75.7	81.4	65.1
NY(Manhat	67.5	76.6	75.0	75.8	73.0	77.8	88.7	88.9	95.6	105.9	82.5
Queens	37.6	36.2	44.3	43.9	42.5	46.9	52.7	51.4	58.6	63.3	47.8
Richmond	49.5	45.3	47.2	47.0	37.0	27.4	30.4	36.1	29.9	42.3	39.0
NYC City	61.3	59.8	63.0	61.8	58.8	63.3	70.2	74.8	85.2	98.6	69.1
Average	40.6	34.6	40.9	36.6	32.4	30.7	34.1	33.2	33.3	35.6	35.3

Higher asthma rates have often been associated with urban living conditions. In order to establish whether high prevalence rates calculated for counties in New York State can be accounted for by this urban effect, a comparison between the hospitalization rate and the urbanity of counties of interest is shown below in Table 3. Relative urbanity is evaluated using population density estimates. It can be noted that this rough approximation does not account for disparities within large counties, such as those comprising New York City, but it can serve as a rough relative measure of the urbanity in a given county. As can be seen in the chart below, many counties with high hospitalization rates are not very urban, while many highly urban counties have relatively low hospitalization rates. Of the nine counties listed with hospitalization rates greater than 50% above average, only Bronx, Kings and New York/Manhattan counties have above average population densities. Thus there must be some other reason that these unurban counties are experiencing high rates of hospitalizations due to asthma.

Table 3: Average Asthma Discharge Rates and Population Densities, by County

County	Ave Pop	Ave Pop /Mi	Ave Prev
Albany	291411.0	556.1	26.6
Allegany	50535.8	49.0	26.3
Broome	212307.8	298.2	14.6
Cattaraug	84729.9	64.9	41.8
Cayuga	81379.1	117.1	30.6
Chautauqu	142523.0	134.0	25.9
Chemung	93669.9	227.9	20.8
Chenango	51137.9	57.0	29.1
Clinton	84460.3	91.0	17.8
Columbia	62446.9	97.9	15.8
Cortland	48510.8	97.0	59.0
Delaware	46908.8	32.6	30.6
Dutchess	257605.8	320.4	24.3
Erie	969359.2	926.7	26.7
Essex	36897.3	20.4	24.8
Franklin	45750.9	27.9	31.6
Fulton	54268.2	109.2	123.2
Genesee	59886.2	121.0	54.9
Greene	44119.3	68.1	15.2
Hamilton	5120.4	3.0	60.1
Herkimer	66150.2	46.7	25.5
Jefferson	102892.3	80.8	45.8
Lewis	26103.2	20.3	24.7
Livingsto	61448.2	37.1	32.9
Madison	68422.9	104.3	25.7
Monroe	711655.4	1073.4	23.3
Montgome	51983.5	128.7	104.4
Nassau	1302384.0	4537.9	27.2
Niagara	219348.0	417.0	49.7
Oneida	251409.2	206.2	22.7
Onondaga	467820.3	536.0	19.9
Ontario	94335.3	146.5	16.1
Orange	298752.5	361.7	45.4
Orleans	41201.6	105.4	27.0
Oswego	120124.3	125.9	28.7
Otsego	59958.3	59.7	38.5
Putnam	93190.4	360.1	32.0
Rensselae	153985.3	235.1	21.5
Rockland	266293.2	1521.7	21.3
St. Lawre	112557.1	41.3	32.3
Saratoga	174980.7	215.0	36.0
Schenecta	149629.6	726.4	29.2
Schoharie	31443.0	50.4	17.1
Schuyler	18427.2	56.0	56.9
Seneca	33374.5	102.1	9.7
Steuben	98372.9	70.5	41.6
Suffolk	1319648.5	1447.0	28.0
Sullivan	68039.9	63.8	29.3
Tioga	51351.5	99.9	9.9
Tompkins	92459.1	193.8	24.7
Ulster	163955.2	145.0	21.0
Warren	57937.2	65.7	39.4
Washingto	58296.5	69.7	34.9
Wayne	88577.1	146.4	29.0
Westchest	875256.7	2000.5	25.9
Wyoming	42186.7	70.9	43.4
Yates	22378.5	56.0	18.4
Bronx	1199923.9	28569.5	97.8
Kings	2303036.5	32900.5	65.1
NY/Manha	1480358.3	67239.0	82.5
Queens	1951315.3	18072.4	47.8
Richmond	378048.9	6407.6	39.0
NY City	7313193.0	24295.3	69.1
Average	239420.3	373.7	35.3

The two counties with the highest childhood hospital discharge rates are Fulton and Montgomery counties, located near each other towards the south of the Adirondack Region in New York State. Though neither counties have high population densities, neither appear to be below average economically (as judged by poverty levels) and neither appears to have poor health care (as judged by number of active physicians), asthma hospitalization rates in these counties are of the same order as rates in notoriously unhealthy Bronx and Kings Counties. Thus further investigations into Fulton and Montgomery counties may provide clues as to possible causes of increased asthma occurrence in children. Furthermore, regions in New York State with high asthma discharge rates can be pinpointed and investigated for further possible explanations as to the increase in asthma prevalence.

2.2.3 Local Estimates for New York State from the National Health Interview Survey

As described above, data from the NHIS cannot be used to generate localized area estimates of childhood hospitalizations. However, the actual counts of hospitalizations due to asthma for age groups 0 - 15 and 0 - 17, by county of residence, for all 39 of 62 total counties sampled in New York State (listed below) in the NHIS were obtained from John Horm of the National Center for Health Statistics. Data for the years 1978 - 1994 were obtained; though statistics for the NHIS have been collected since 1957, problems would be encountered in obtaining direct counts for years prior to 1978 since this data was recorded on punchcards that are difficult to locate. Horm was not able to give me sampling weights, due to confidentiality issues. However, since the calculations for which this data were used involve working within samples and not the generation of larger area estimates, national weights are probably unnecessary for my calculations. Alternatively, Horm could have provided weighted prevalence rates for each county sampled, but then actual counts would not have been able to be seen and error estimates would not have been able to be calculated, if necessary. Thus, the actual numbers of cases of asthma and numbers of people sampled in the given age groups were themselves analyzed. Rates were calculated as the number of discharges per the number at risk investigated by the survey. Due to the number of counties in New York State sampled, and the small number of children in this age group sampled within each county, the data obtained is very sparce and lends to questionable accuracy. Though it was already known that this data would not be representative on a state-wide level, its validity on a county wide level has also been shown to be questionable.

Analysis of this data showed similar trends for the 0 - 15 cohort and the 0 - 17 cohorts; hence, further analyses were conducted using data for the 0 - 17 cohort in order to include as

many data points as possible. The patterns for individual counties are very hard to observe, due to a lack or sparcity of data for many of the counties. For example, counties in the survey were not necessarily consistently surveyed for all years in the 1978 - 1994 time period. The survey never included Fulton County, and only sampled Montgomery County four times, during the given time period. In an attempt to account for this sparcity of data, average rates over several year time periods and for larger regions within New York State were calculated. Table 4 shows average rates over the time periods listed therein. Values are given as number of people surveyed who reported asthma in the given age group per number of people surveyed in that age group, for each county. Blanks indicate that no samples were taken during that time period. Reliable trends still prove difficult to discern, and data is sparce for some counties even when multiple years are considered together.

As can be seen in Table 4, the prevalence rates for both cohorts exhibited an overall increase between 1978 - 1994, despite a drop in 1986 and 1987. The average rate of hospitalization for the 0 - 17 age strata is 0.0537. Counties exhibiting an average rate greater than 50% above average (0.0806) are Montgomery(0.25), Orleans (0.25), Oswego (0.095), Bronx (0.088), and Clinton (0.085). Counties exhibiting an average rate greater than 25% above average (0.067) are Erie (0.078), New York/Manhattan (0.078), Niagara (0.069), Orange (0.068), Rockland (0.068), Albany (0.068), and Tompkins (0.062).

All counties were placed in one of four regions; those counties for which NHIS data were available were used to give regional estimates from this data, and are asterisked below. Comparisons between different regions have the ability to show the influence of different pollutants in different areas.

East	*Middle*	*North*	*Southwest*
Allegany	Broome*	Clinton*	Albany*
Cattaraugus	Cayuga	Essex	Columbia*
Chautauqua*	Chenango	Franklin	Delaware*
Chemung*	Cortland	Hamilton	Dutchess*
Erie*	Madison*	Herkimer*	Fulton
Genesee	Oneida*	Jefferson	Greene*
Livingston*	Onondaga*	Lewis	Montgomery*
Monroe*	Oswego*	St. Lawrence	Orange*
Niagara*	Tioga*	Warren	Otsego
Ontario*	Tompkins*		Putnam*
Orleans*			Renssalaer*
Seneca	*City*		Rockland*
Steuben*	Bronx*		Saratoga*
Wayne*	Kings*		Schnectady*
Wyoming	Nassau*		Schoharie
Yates	New York (Manhattan)*		Sullivan
	Queens*		Ulster
	Richmond*		Washington
	Suffolk*		Westchester*

Results of the regional analysis are shown in Table 4 below. An increase from 1979 to 1983 occurs in all five regions. The average rate in the East (0.0572), Middle (0.053), North (0.042), Southwest (0.041) and City (0.066) regions are all similar, and none are significantly greater than the state average (0.054). Again, these calculations are most likely inaccurate, since not enough counties were sampled in each region to give reliable representations of those regions.

Table 4: Asthma Discharge Rates from Direct Counts obtained by the NHIS, by Region and County, 1978 - 1994

	Approx Ave	1978-1980	1981-1985	1986-1990	1991-1994
East					
Niagara	0.07	0.00	0.09	0.00	0.17
Erie	0.08	0.05	0.04	0.10	0.12
Chautauqua	0.05	0.08	0.03		
Orleans	0.25	0.00	0.50		
Monroe	0.06	0.05	0.08	0.08	0.00
Livingston	0.02		0.03	0.00	0.00
Wayne	0.03		0.07	0.00	0.00
Ontario	0.00			0.00	0.00
Steuben	0.02	0.00	0.04		
Chemung	0.00	0.00	0.00		
Ave	0.06	0.02	0.10	0.03	0.05
Middle					
Tompkins	0.06	0.00	0.13		
Tioga	0.00	0.00	0.00		
Onondaga	0.04	0.02	0.06	0.02	0.06
Oneida	0.02	0.00	0.05	0.00	0.02
Madison	0.16	0.25	0.10	0.00	0.33
Broome	0.03	0.08	0.00		
Ave	0.05	0.04	0.09	0.02	0.06
North					
Clinton	0.09		0.00	0.06	0.13
Herkimer	0.00	0.00	0.00	0.00	0.00
Ave	0.04	0.00	0.00	0.03	0.06
Southwest					
Montgomery	0.25			0.00	0.50
Saratoga	0.00	0.00	0.00	0.00	0.00
Schnectady	0.03	0.00	0.00	0.01	0.08
Delaware	0.01	0.03	0.00		
Albany	0.07	0.00	0.04	0.03	0.18
Greene	0.00			0.00	0.00
Rensselaer	0.00	0.00	0.00	0.00	0.00
Columbia	0.00	0.00			
Dutchess	0.00	0.00	0.00		
Orange	0.07	0.08	0.03	0.12	0.04
Putnam	0.02	0.00	0.00	0.08	0.00
Rockland	0.07	0.00	0.17	0.00	0.08
Westcheste	0.03	0.03	0.05	0.00	0.04
Ave	0.04	0.01	0.03	0.02	0.09
City Region					
Bronx	0.09	0.11	0.09	0.04	0.14
NY (Manhat	0.08	0.06	0.07	0.09	0.09
Kings	0.05	0.03	0.06	0.04	0.06
Richmond	0.04	0.05	0.06	0.05	0.00
Queens	0.05	0.03	0.04	0.05	0.06
Nassau	0.06	0.02	0.08	0.05	0.05
Ave	0.06	0.05	0.07	0.05	0.07
Total	0.05	0.04	0.05	0.05	0.07

The above considerations suggest that direct counts per number at risk obtained from the NHIS are not useful in studying hospitalization patterns for asthma. A comparison with asthma inpatient discharge data available from the New York State Department of Health further supports this finding. Counties with high discharge rates as calculated directly by NHIS counts do not correlate with most of the counties found to have high discharge rates from New York State Biometrics data. Since it provides a much more complete and statistically valid data set, rates obtained from the New York State DOH can be assumed to be more accurate than those obtained from actual NHIS counts. Hence, due to the limited usefulness of actual NHIS counts, the search for the data collected prior to 1978 was not pursued, and the calculations performed were not considered reliable sources of information. The NHIS proves to be a valuable source of regional and national hospitalization rates, but does not appear to provide accurate estimates of county or state hospital discharges due to asthma.

2.2.4 County Estimates from the National Health Interview Survey

Estimates by county of childhood and adult asthma prevalence in 1993 for each state of the United States have been published by the American Lung Association. These estimates were derived from the national estimates given in the National Health Interview Survey, using specific age distributions in each county. The prevalences derived by these calculations provide estimated numbers of people with asthma in given states or counties; however, prevalence rates cannot be calculated from this data. In order to do so, each estimated prevalence would need to be divided by the estimated population in each county or state. Due to the analytical methods used to derive these state and county estimates, such manipulations would all return the same number from which local estimates were first derived. Thus, though these estimated prevalences may prove very useful to health care administrators within a particular state or county, they cannot be used to estimate local area asthma rates or to compare trends in asthma prevalence between different states and/or counties.[35]

2.2.5 Analysis of Mortality Statistics

County based mortality records can be obtained from the Vital and Health Statistics Series published by the National Center for Health Statistics. As described above, the data from 1968 - 1978 lists deaths due to bronchitis, emphysema and asthma (ICD codes 490 - 493, explained below), while that for 1979 - 1991 covers deaths due to chronic obstructive pulmonary

[35] American Lung Association. Estimated Prevalence and Incidence of Lung Disease by Lung Association Territory. May 1996, and Telephone conversation with Alexandra Gorman of the ALA, May 1997.

disease and allied conditions (ICD 490 - 496, including asthma). Such data was collected for all counties in New York State, in an effort to analyze any trends which could be observed in this data and to evaluate if these statistics could be representative of prevalence trends.

Average mortality rates for all counties in New York State are shown in Tables 7 and 8, below. Values shown are rates per 10,000. Counties in which mortality rates due to the relevant respiratory disorders were greater than 25% above average (1.8) during 1968 - 1978 are as follows, in descending order: Fulton (3.24), Hamilton (3.17), Steuben (2.74), Franklin (2.66), Schuyler (2.4), Columbia (2.34), Cattaraugus (2.34), Wyoming (2.31), and Montgomery (2.28). These counties all show increasing trends over the relevant time brackets, with the exception of Hamilton county. Counties with greater than 25% above average (3.74) during 1979 - 1991 are Hamilton (6.2), Steuben (5.3), Franklin (5.3), Delaware (5.2), Cayuga (4.8) and Fulton (4.7).

Table 7: 1968 - 1978 Average Mortality Rates per 10,000

Year	68-72 ave	73-78 ave	68 - 78 ave
Albany	1.85	1.42	1.62
Allegany	2.53	1.30	1.86
Broome	1.86	1.55	1.69
Bronx	1.12	0.91	1.00
Cattaraug	2.11	2.53	2.34
Cayuga	1.71	1.32	1.50
Chautauqu	1.74	1.79	1.77
Columbia	2.67	2.07	2.34
Cortland	2.45	1.47	1.91
Clinton	1.53	1.23	1.36
Delaware	2.00	2.19	2.10
Erie	1.80	1.59	1.68
Franklin	3.16	2.24	2.66
Fulton	3.60	2.94	3.24
Genesee	2.26	1.64	1.92
Green	2.27	1.67	1.94
Kings	1.05	0.72	0.87
Hamilton	3.44	2.95	3.17
Herkimer	1.94	1.90	1.92
Jefferso	2.20	1.56	1.85
Lewis	1.35	0.93	1.12
Montgome	2.61	2.02	2.28
Nassau	0.77	0.69	0.72
Niagara	1.65	1.55	1.60
NY(Manha	1.51	0.95	1.21
Oneida	1.81	1.94	1.88
Onondaga	1.17	0.94	1.04
Orange	1.85	1.46	1.64
Orleans	2.48	1.86	2.14
Otsego	1.93	2.08	2.02
Queens	1.07	0.83	0.94
Richmond	1.01	0.83	0.91
Saratoga	2.12	1.35	1.70
Schnectac	1.74	1.66	1.69
Schuyler	2.68	2.17	2.40
Steuben	3.35	2.23	2.74
Suffolk	0.93	0.71	0.81
Wyoming	2.00	2.56	2.31
Warren	2.63	1.78	2.17
Washingt	1.85	1.83	1.84
Average	1.99	1.63	1.80

Table 8: 1979 - 1991 Average Mortality Rates per 10,000

Year	79 - 81 ave	82 - 86 ave	87 - 91 ave	79 - 91 Ave	84 - 91 Ave
Albany	2.95	3.59	3.76	3.51	3.83
Allegheny	2.89	3.97	5.03	4.13	4.75
Broome	2.92	3.97	5.06	4.15	4.76
Bronx	2.03	2.29	2.24	2.21	2.32
Cattaraugus	2.68	4.14	5.31	4.26	4.92
Cayuga	3.29	4.60	5.87	4.78	5.71
Chautauqua	2.91	3.96	5.00	4.12	4.67
Columbia	3.09	4.34	4.31	4.04	4.31
Cortland	4.20	3.56	5.35	4.40	4.74
Clinton	2.15	2.52	3.39	2.77	3.09
Delaware	3.84	5.06	6.09	5.18	5.87
Erie	2.75	3.34	3.86	3.40	3.78
Franklin	4.55	4.46	6.60	5.30	5.94
Fulton	4.57	4.70	4.80	4.71	4.85
Genesee	2.13	3.46	3.83	3.30	3.76
Green	2.04	4.20	4.19	3.69	4.53
Kings	1.55	1.87	2.16	1.91	2.07
Hamilton	3.30	9.41	4.63	6.16	6.48
Herkimer	3.80	4.04	4.64	4.22	4.72
Jefferson	2.84	4.77	4.77	4.32	4.82
Lewis	3.04	3.93	3.78	3.67	4.11
Montgomery	3.06	4.46	3.70	3.85	4.11
Nassau	1.63	2.12	2.58	2.18	2.46
Niagara	2.91	3.91	4.28	3.82	4.12
NY(Manhattn)	2.16	2.26	2.37	2.28	2.35
Oneida	2.93	3.76	3.93	3.64	4.04
Onondaga	2.79	3.17	3.49	3.21	3.47
Orange	2.57	3.01	3.30	3.02	3.25
Orleans	3.29	3.72	3.50	3.54	3.74
Otsego	4.11	4.37	4.78	4.47	4.86
Queens	1.76	1.93	2.20	1.99	2.15
Richmond	2.32	2.62	2.75	2.60	2.71
Saratoga	2.18	3.15	2.92	2.84	3.12
Schnectady	2.69	3.32	4.37	3.58	3.98
Schuyler	4.48	3.67	4.90	4.33	4.43
Steuben	3.96	5.04	6.44	5.33	5.76
Suffolk	1.76	2.53	3.32	2.65	3.14
Wyoming	3.82	3.94	4.29	4.05	4.37
Warren	3.21	3.53	4.77	3.93	4.32
Washington	3.58	4.29	4.34	4.14	4.26
Tot Ave	2.97	3.77	4.17	3.74	4.12

Table 8 also shows average mortality rates form 1984 to 1991. Counties with rates greater than 25% above average are in the following descending order: Hamilton, Franklin, Delaware, Steuben, and Cayuga. These data do not correlate with the order of counties with high childhood hospital discharge rates calculated from New York State DOH statistics: in descending order, Fulton, Montgomery, Bronx, New York/Manhattan, Kings, Hamilton, Cortland, Schuyler and Genesee. New York State county mortality rates from the Vital and Health Statistics do not seem to correspond to county childhood hospital discharge rates for asthma. Thus, mortality statistics from the NCHS do not provide a very accurate representation of childhood inpatient asthma discharges. Assuming that the latter is a more accurate estimate of asthma prevalence, mortality statistics from the NCHS were not further considered as a source of information on relative asthma prevalence amongst counties, in this research.

State wide mortality statistics for asthma by county or zip code can be obtained directly from most state departments of health. Mortality rates from 1944 - 1995 have been obtained for the state of Minnesota, for example, and show an increase in the state average between 1971 - 1995. Four counties: Aitkin, Chippewa, Nobles and Wadena, show an increase after 1980. Difficulties in estimating prevalence from such data have been discussed previously. Further difficulties when considering mortality statistics from different states include the fact that different states might follow varied practices in reporting causes of mortality. Prevalence estimates from mortality statistics would probably not be accurate enough to use in comparisons of asthma occurrence between different counties or states. Nevertheless, if time provided, such analyses would give local area mortality trends which may prove useful in understanding the rise in asthma prevalence.

2.2.6 Regional Estimates of Asthma Hospital Discharge Rates

Regional estimates of the number of discharges due to asthma from short-stay, non-Federal hospitals are given by the National Hospital Discharge Survey Series #13, from the National Center for Health Statistics. This appears to be the only single source with somewhat local area hospitalization estimates for the entire nation. In this series, the United States is divided into four regions consisting of the following states: the Northeast: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont; the Midwest or North Central: Illinois, Iowa, Indiana, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin; the South: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland,

Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia; and the West: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Nevada, New Mexico, Oregon, Utah, Washington, West Montana, and Wyoming. Regional data is available in the form of the number of patients for whom one of their top three diagnoses included asthma (all listed diagnoses) for 1971 - 1975 and 1978 - 1993 and for the subset for whom the primary diagnosis was asthma (first listed diagnoses) for 1965, 1968, 1971 - 1975, and 1978 - 1993.

As with national statistics, adjustments for asthma data using ICD8/ICD9 comparability ratios is only accurate when done at the total population level, and thus is not meant to be done in order to analyze subgroups within the total population. However, I have assumed that it is somewhat accepatable to use this correction factor in the analysis of regional data, since Evans, III et. al[36]. use this comparability ratio to give adjusted values for age and racial cohorts. This is one source of error in our estimate of prevalence trends based on hospitalization data. Again, no corrections were performed for data from ICD7 when comparing it to that from ICD8, in following the methods used by Evans, III et al. As stated previously, the change in ICD codes for asthma may reflect changes in accepted definitions of the disorder, or in criteria used in diagnosis of asthma. These changes are not quantitatively accounted for, though they may have slightly contributed to increases observed in asthma rates.

Rates and counts are available for all listed diagnoses, from which regional populations were calculated and applied to first listed diagnoses in order to give rates for the latter. First listed diagnosis rates for 1965 were calculated using population estimates published by the US Bureau of theCensus. As can be seen in Figures 2 and 3, both all listed and first listed diagnoses rates show a generally increasing trend for all regions until the 1990s, at which point a leveling off occurs in all regions but the Northeast. The Northeast continues to increase during the 1990s, and has visibly higher rates than the other regions. Average first listed and all listed diagnoses rates, corrected to ICD8 where applicable, are given in Table 9 below.

Table 9: Average All Listed and First Listed Asthma Diagnoses by Region

	All Listed per 100,000					First Listed per 100,000				
	Total US	NE	MidW	South	West	Total US	NE	MidW	South	West
1968						69	66	76	66	65
1971-1980	137.0	134.2	144.7	137.5	130.2	86.9	89.8	90.6	84.8	83.7
1981-1989	197.9	219.8	212.1	187.2	175.4	121.7	133.4	128.7	118.6	106.3
1990 - 1993	233.7	317.2	244.1	209.5	179.2	118.6	150.7	123.8	110.1	95.3
Total Ave	181.5	205.7	192.5	172.6	158.9	106.1	117.6	111.6	102.1	94.2

[36] Evans, III, et. al., 1987.

Figure 2: All Listed Diagnoses

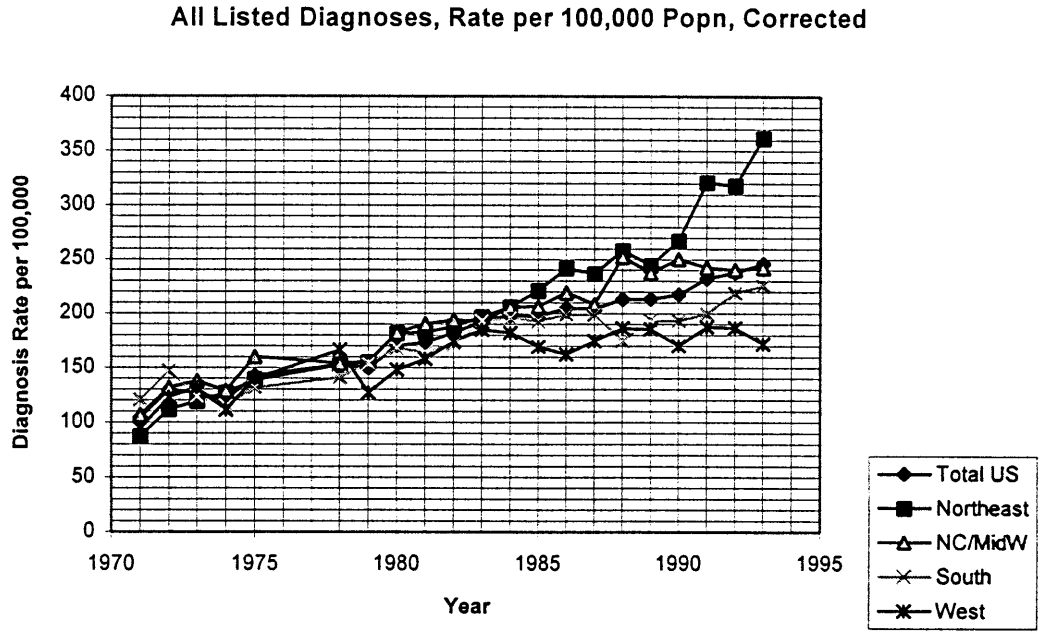
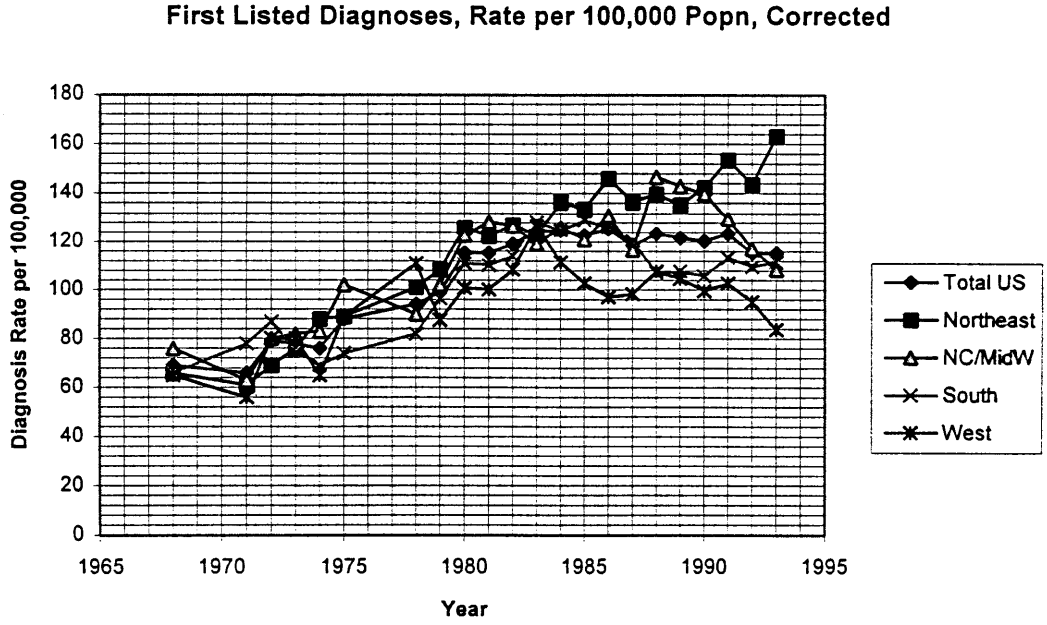


Figure 3: First Listed Diagnoses



Chapter 3: History of Lanthanide Usage and Exposure

The lanthanides make up the 8th row of the periodic table, and consist of lanthanum (La, atomic number 57), cerium (Ce, atomic number 58), praseodymium (Pr, atomic number 59), neodymium (Nd, atomic number 60), promethium (Pm, atomic number 61), samarium (Sm, atomic number 62), europium (Eu, atomic number 63), gadolinium (Gd, atomic number 64), terbium (Tb, atomic number 65), dysprosium (Dy, atomic number 66), holmium (Ho, atomic number 67), erbium (Er, atomic number 68), thullium (Tm, atomic number 69), ytterbium (Yb, atomic number 69), and lutetium (Lu, atomic number 71). The lanthanides all have similar properties, and have come to be called the rare earth elements, due to the difficulty in separating them from each other and not to an overwhelming absence from crustal matter.

3.1 Sources of Lanthanide Emissions

Mixtures of rare earth elements are used in various quantities in many manufacturing processes. Industrial use of the lighter lanthanides began to increase a few decades ago with the addition of lanthanum into the zeolite cracking catalysts of petroleum refineries. By 1969, lanthanides, predominantly lanthanum, were used in over 90% of catalytic cracking units in such refineries. Though lanthanide emissions from these refineries themselves may not be significant, increased exposure may occur through the use of residual fuels produced by these refineries, such as Number 6 oil, in oil-fired power plants. Lighter fuels which are used for other purposes such as in heating houses or fueling motor vehicles are not likely to have retained significant amounts of lanthanides during refining. Thus lanthanide emissions probably began to be released both from petroleum refineries as well as from the oil-fired power plants which burned petroleum from these refineries, in the late 1960s. Furthermore, in 1981 lanthanides began to be used in motor vehicle catalytic converters, providing an additional source of predominantly lanthanum and cerium. Lanthanide usage partially decreased begining in the 1980s due to a reduction in the concentration used in cracking catalysts.[37] Increased lanthanide concentrations have been documented in fine aerosol particles from regions expected to be influenced by oil-fired power plants and refineries, suggesting that uses of lanthanides by these industries increase human exposures to these metals. Motor vehicle emissions may play a more significant role in regions not under the influence of oil-fired power plants than in those regions affected by oil-fired power

[37] Kitto, Michael E. Anderson, David L., Gordon, Glen E. and Olmez, Ilhan. Rare Earth Distributions in Catalysts and Airborne Particles. Environmental Science Technology. 1992, 26: 7, 1368 - 1375.

plant emissions.[38] Thus lanthanide emissions have gradually impacted atmospheric particulate concentrations since the middle 1960s.

The size of the lanthanide particles emitted would be expected to play a role in the effect on the human population of such emissions. Particulate matter is defined as particles having a diameter of 10 μm or less, and are likely to able to be inhaled past the upper airways. Particles which are 2.5 μm (PM2.5) or less are referred to as fine particulate mass, and are likely to be collected in the lung alveoli, bronchioles, or other peripheral regions. These particles are generally longer living, and travel further from the point of emission. Those particles which fall within the range of 2.5μm - 10 μm (PM2.5 - PM10) are referred to as coarse particulate mass and are likely to collect in the bronchial airways. Coarse particles settle quicker and thus usually remain in the area of the source of emission. Petroleum refineries emit relatively large concentrations (3300 ppm La) in fine particles, and thus may have a larger regional impact. Oil-fired power plants emit relatively large concentrations of lanthanides in both fine particles (290 ppm La) and in coarse particles (3875 ppm), and thus may have a somewhat significant regional impact, and a larger local impact.[39,40] The effect of lanthanides due to motor vehicles is most likely more distributed over large areas, since they travel from place to place, even though larger amounts of coarse lanthanum particles are emitted than of fine particles.[41] The exposure due to refineries is not expected to play as large a role as that due to oil-fired power plant or motor vehicle emissions, and therefore has not been investigated in detail.

3.2 Estimated Measures of Lanthanide Emissions

Direct measures of lanthanide emissions are generally not available. However, relative emissions can be estimated using various statistics from the petroleum and minerals industry, as listed below. All sources of data for which state estimates are given can be used to find regional estimates corresponding to the regions used in the National Hospital Discharge Survey. Analysis of each statistical source is described below. Comparisons with asthma statistics are shown in Chapter 4.

3.2.1 Lanthanide Usage in Catalysts

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[38] Olmez, I and Gordon, GE. Rare Earths: Atmospheric Signatures for Oil-Fired Power Plants and Refineries. Science. 229, September 6, 1985, 966 - 968.

[39] references in Schwartz, J, Dockery, DW, and Neas, LM. Is Daily Mortality Associated Specifically with Fine Particles? Journal of the Air & Waste Management Association. 46, October 1996, 927 - 939.

[40] Olmez, I, Sheffield, AE, Gordon, GE, Houck, JE, Pritchett, LC, Cooper, JA, Dzubay, TG, and Bennett, RL. Compositions of Particles from Selected Sources in Philadelphia for Receptor Modeling Applications. JAPCA. November 1988, 38: 11, 1392 - 1402.

[41] Huang et al., 1994.

National statistics of lanthanide usage in catalysts are available from the U.S. Bureau of Mines Mineral Yearbook, dating back to 1965. Data from 1965 - 1991 were analyzed, excluding 1966, 1979, 1988, and 1989, and show an increase in usage in the United States until 1984, at which point usage drops drastically. This decrease is most likely due to a drop in the percentage of rare earths used in petroleum refinery zeolite cracking catalysts.[42] Cumulative averages clearly show this increase and then decrease, as can be seen in Table 10 below. All values are in 1000 REO eq.

Table 10: Average Lanthanide Usage in Catalysts

Time Period (years)	Ave Usage (10^3 REO eq)	Time Period (years)	Ave Usage (10^3 REO eq)
1965 - 1969	2.50	1965 - 1970	3.04
1970 - 1980	6.44	1971 - 1980	6.58
1981 - 1991	7.87	1981 - 1984	11.59
		1985 - 1991	4.89

This is the most direct measure of lanthanide exposure available. Unfortunately, to my knowledge, more local-area estimates of usage cannot be obtained. All other estimates of lanthanide emissions are more indirect, since they are based upon energy sources from which emissions may have been released and not upon any measure of lanthanide use by that energy source. Thus trends from these estimates reflect the use of that energy source, not changes in the amounts of lanthanides used by those sources.

3.2.2 Lanthanide Emissions from Oil-fired Power Plants

3.2.2.1 Power Generated by Oil

Power generated by fuel oil can serve as an estimate of the activity of oil-fired power plants in the United States. Such statistics are available from the Edison Electric Institute, in terms of kilowatt-hours of energy generated by fuel oil, and have been analyzed for data from 1954 - 1994 at both the state and regional level. Available statistics use preliminary estimates for 1974 - 1976 and 1988 - 1991, and include petroleum coke usage beginning in 1983. Population normalized regional estimates of power generated by fuel oil could be done to provide a means of comparing potential exposure in the four regions of the US, and would probably reveal a significant relatively higher usage in the Northeast and relatively lower usage in the Midwest.

[42] Wainwright, NA, Thilly, W, and Olmez, I. Increased Atmospheric Levels of Lanthanides as a Potential Cause of the Change in Epidemiology of Childhood Asthma. Center for Environmental Health Sciences and NRL, Environmental Research and Radiochemistry, Massachusetts Institute of Technology.

Concentrations of La and Ce emissions from two petroleum refineries have been obtained by Olmez et.al, and are normalized using the power at which the refineries were run, to give emissions/MW. Fine particle emissions from Eddystone and Schuylkill were calculated to be 0.329 ppm/MW and 0.978 ppm/MW for La, and 0.225 ppm/MW and 0.783 ppm/MW for Ce, respectively, giving an average estimate of 0.654 ppm/MW La and 0.504 ppm/MW Ce fine particulate emissions. Coarse particle emissions from Eddystone and Schuylkil were calculated to be 4.43 ppm/MW and 13.0 ppm/MW for La and 1.37 ppm/MW and 7.61 ppm/MW for Ce, respectively, giving an average estimate of 8.74 ppm/MW La and 4.49 ppm/MW Ce coarse particulate emissions.[43] Since the concentrations used are averages, the time over which they were taken does not need to be taken into accoutn. There may be heterogeneity in the emissions from different power plants and at different times, though this average. The average concentrations in fine and coarse particles can be used to calculate estimated exposures due to oil-fired power plants. The power generated by fuel oil is multiplied by the average concentrations of La or Ce emitted by petroleum refineries. Regional averages of the total lanthanum plus cerium concentrations in fine and coarse particles are shown below in Tables 11 and 12. Concentrations are in terms of Kwhr * ppm/Kw. This number does not give the value for an actual physical concentration, but does provide relative concentrations which can be compared across the United States.

Changes in the amounts of lanthanides used by oil-fired power plants are not reflected in this data series, since only one set of emission estimates from 1988 were used. Pre-1965 estimates are shown, though lanthanides were not used during this time period. Thus this data should only be used to estimate regional lanthanide emissions from oil-fired power plants following 1965.

Table 11: La + Ce Concentrations in Fine Particles

Region	54 - 59 average	60 - 64 average	65 - 68 average	70 - 80 average	81 - 89 average	90 - 94 average	54 - 94 average
NE	17.29	27.37	63.85	136.41	96.15	55.38	73.99
MidW	1.82	1.48	1.97	23.28	5.91	3.66	8.03
South	12.06	12.61	26.19	113.92	48.95	47.45	50.58
West	13.66	16.69	17.99	69.99	20.10	11.16	29.24
Tot US	44.82	57.69	110.00	343.59	172.38	117.65	162.02

[43] Olmez et. al., 1988.

Table 12: La + Ce Concentrations in Coarse Particles

Region	54 - 59 average	60 - 64 average	65 - 68 average	70 - 80 average	81 - 89 average	90 - 94 average	54 - 94 average
NE	197.56	312.70	729.42	1558.36	1098.41	632.70	845.23
MidW	20.74	16.85	22.52	265.91	67.49	41.77	91.78
South	137.75	144.10	299.17	1301.36	559.20	542.08	577.84
West	156.01	190.68	205.56	799.52	229.66	127.44	333.99
Tot US	512.06	659.03	1256.68	3925.16	1969.28	1344.01	1850.87

Total concentrations in both fine and coarse particles are significantly higher in the Northeast than in all other regions, and the distinction remains significant even after normalizing to regional area. The Northeast also shows a significant increase until 1973, a peak from 1973 - 1978, followed by a significant decrease until a leveling of around 1984.

3.2.2.2 Percent of Power Generated by Oil, Coal and Gas

National, state and average regional percentages of power generated by various sources are available for 1984 - 1994. These percentages can be used to determine whether a given state is currently under the influence of oil-fired power plants and/or of coal and gas fired power plants. In the table below, those states or regions which are expected to be significantly influenced by fuel oil emissions from within that state or region are highlighted, while those which may be somewhat influenced by fuel oil emissions within that state or region are underlined. Potential influence by fuel oil emissions are determined regardless of potential influence due to coal and gas emissions; however, in order to be more complete, percent of power generated by the latter are also listed in the table below. Emissions from oil-fired power plants would be expected to have a large influence in the Northeast, while having a negligible influence in the Midwest. The South and West are more mixed regions, in which some states may be influenced by oil emissions, while some states would not be influenced at all.

3.2.2.3 Lanthanide Concentrations in Residual Fuel Oil

The amount of residual fuel oil consumed by state per year is available for the years from 1986 - 1993 from the American Petroleum Institute Basic Petroleum Data Book. Using the concentrations of lanthanum and cerium found by Olmez in nine Number 6 fuels from Florida Power and Light[44], amount (mass) of potential emissions of lanthanum and cerium from residual fuel oil burned in oil-fired power plants can be estimated. Since the lanthanide concentrations are

[44] Olmez, I. Personal communication.

given in ppm (μg/gr), the amount of fuel oil consumed must be converted from the volume given in barrels to a unit of mass. The density of petroleum used for this conversion was 0.9660 kg/dm3, at 15 C, given an API value of 15.5 for No. 6 fuel.[45,46] Calculated amounts are given below in Table 13, in thousands of kilograms. Over the whole time period, a slight decrease is seen in Northeast, over the whole time period.

Table 13: La + Ce in Residual Fuel Oil

1986 - 1993 Average	Northeast	Midwest	South	West	Total US
Total emissions (La + Ce , kg)	25838	2481	22572	13683	64504

3.2.3 Lanthanide Emissions from Motor Vehicles

Though the amount of lanthanides in motor gasoline is negligible, motor gasoline consumption by state can be used as a gage of motor vehicle catalytic converter activity in that area. Estimates of lanthanum emissions from motor vehicles have been given by Huang et. al.[47] and are used to calculate relative exposures to lanthanum from motor vehicles. Exposure to cerium from motor vehicles could not be calculated, however, since estimates of cerium emissions from motor vehicles are not as statistically accurate. Measures of emissions are calculated by multiplying the amount in gallons of motor gasoline consumed, by the mass of lanthanum in $1m^3$ of air. Consequently, these manipulations do not give meaningful absolute values, though they do provide relative estimates of exposure from motor vehicles. The relative amounts of emissions of both fine and coarse lanthanum particles are, 1 in the Northeast; 1.4 in the Midwest; 2.2 in the South; 1.2 in the West; and 5.8 in the Total US. Usage of post - 1981 motor vehicles is also estimated using numbers of new car registrations in 1980, 1985, 1990 and 1995. The population normalized number of passenger new car registrations was close to average in all four regions, with the Northeast the highest and the West the lowest.

Chapter 4: Comparisons between Asthma Hospitalization Rates and Estimates of Lanthanide Emissions

In order to investigate whether a causal relationship exists between the increase in lanthanide emissions and the rise in asthma prevalence, a comparison between specific national and regional trends in both must be conducted. If such a relationship is present, asthma rates

[45] Perry, RH, Green, DW, and Maloney, JO, editors. Perry's Chemical Engineering Handbook, 6th Edition. New York: McGraw-Hill Book Company, 1984.
[46] Bolz, RE, and Tuve, GL, editors. CRC Handbook of Tables for Applied Engineering Science, 2nd Edition. Florida: CRC Press, Inc, 1973.
[47] Huang, X, Olmez, I, Aras, NK and Gordon, GE. Emissions of Trace Elements from Motor Vehicles: Potential Marker Elements and Source Composition Profile. Atmospheric Environment. 1994, 28: 8, 1385 - 1391.

would follow the same patterns as lanthanide usage or emissions at both national and regional levels. As explained in Chapter 3, though some of the measures of lanthanide emissions calculated do not provide meaningful absolute concentrations, these figures show relative trends on the nationwide or regional levels, and can thus be compared with trends in asthma prevalence. In general, if a causal relationship does exist, expected trends in asthma would show an increase during the late 1960s, due to the introduction of lanthanides into the petroleum industry, a possible further increase in 1981, due to the additional use of lanthanides in motor vehicles, and finally a possible drop around 1984 due to the drastic reduction in lanthanide usage. This last decrease may not be reflected in asthma rates, however, since usage in motor vehicles has continued into the present.[48] Furthermore, since increased levels of lanthanides in a given time period could affect asthma rates in later time periods, changes in lanthanide emissions not reflected in asthma rates might not be proofs of a lack of correlation.

A causal relationship between lanthanide emissions and asthma levels cannot be proved by analyses at the national, regional or state levels, since these geographical areas are too large and under the influence of too many other factors for such a correlation to be conclusive.[49] Any associations which might be found might support or suggest such a causal relationship, though they could not prove one conclusively. More local relationships must be studied in order to prove such a relationship, and various other factors such as socioeconomic status, population demographics, availability of adequate health care, wind patterns and abundance of pollens/vegetation must be taken account of in such an analysis. However, since more local estimates of asthma prevalence dating back to the 1960s are difficult to obtain, national and regional estimates have been used to investigate the possibility of an association between asthma prevalence and lanthanide emissions.

Yearly plots of asthma rates and of lanthanide emissions are shown on the same graphs in order to allow comparisons between each. Graphs of hospitalization rates as dependent variable and lanthanide emissions as independent variable are also shown. Microsoft Excel was used to generate linear fits and slopes to this data, using the "least squares" method of regression analysis. A positive slope is expected to suggest a causal relationship between the two factors. A negative slope would indicate that increased emissions cause less asthma. Since the latter seems unlikely, we take negative slopes to be coincidental or artifactual and therefore insignificant. Thus, we have only looked at whether positive correlations are suggested or not.

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[48] Kitto, 1990 draft.
[49] vanEenwyk, Juliet. Washington Department of Health. Noninfectious Disease Epidemiology. Telephone conversation, April 1997.

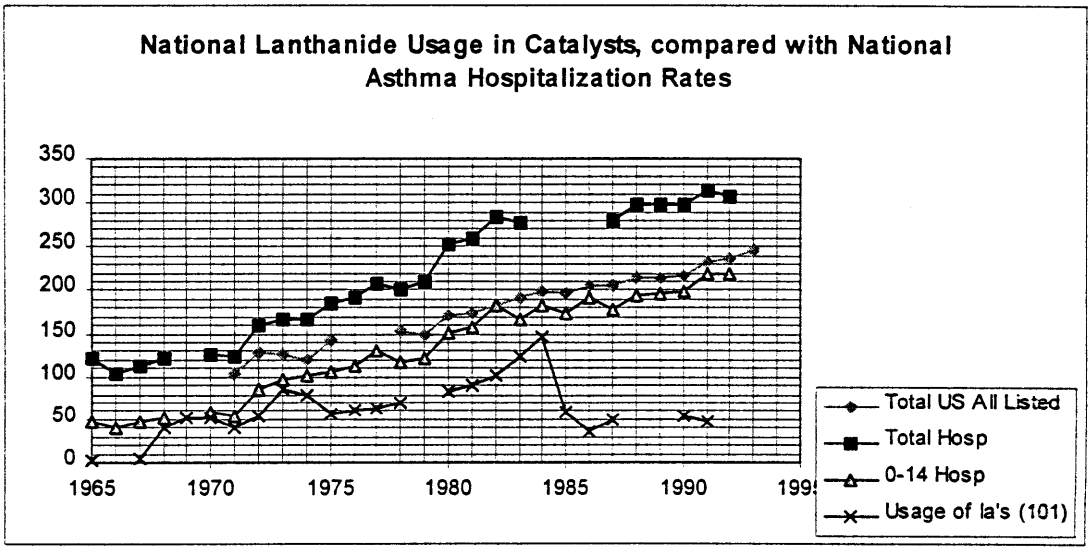
The physiologic distribution of lanthanides in human beings and the mechanisms by which lanthanide exposure could induce asthma are unknown. Hence, it is not clear whether increased levels of exposure would lead to continued increases in asthma prevalence, or if any amounts of lanthanides above a given threshold would induce asthma. If the latter is true, then even when lanthanide emissions drop, increases in asthma rates could still be observed, if the exposure to lanthanides remained above this unknown threshold.

4.1 National Asthma Rates versus Nationwide Exposure to Lanthanides

4.1.1 National Lanthanide Usage

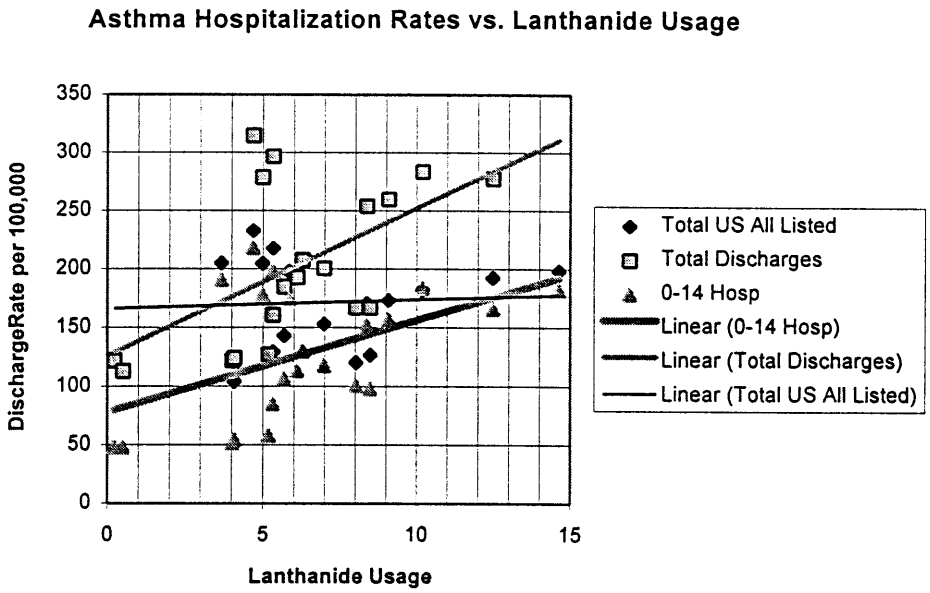
The national usage of lanthanides in catalysts and national hospitalization rates for asthma seem to rise with the same trend until 1984, at which point the use of lanthanides drops without a correlating decrease in asthma hospitalization rates. This indicates either that there is no causative effect, or that the effect of exposure to lanthanides prior to 1985 can still be seen in the 1990s.

Figure 4: National Lanthanide Usage in Catalysts and Asthma Discharge Rates



National hospitalization rates can be plotted against lanthanide usage. Linear plots with increasing slopes would suggest a causal relationship between the two variables. Linear fits can be generated to these graphs, giving slopes of 0.8 for total all listed diagnoses, 7.84 for 0-14 year old hospitalizations, and 12.65 for total hospitalizations. Though these fits are not very accurate, they suggest a possible relationship between lanthanide usage and asthma hospitalizaton rates.

Figure 5: National Asthma Discharge Rates versus Lanthanide Usage

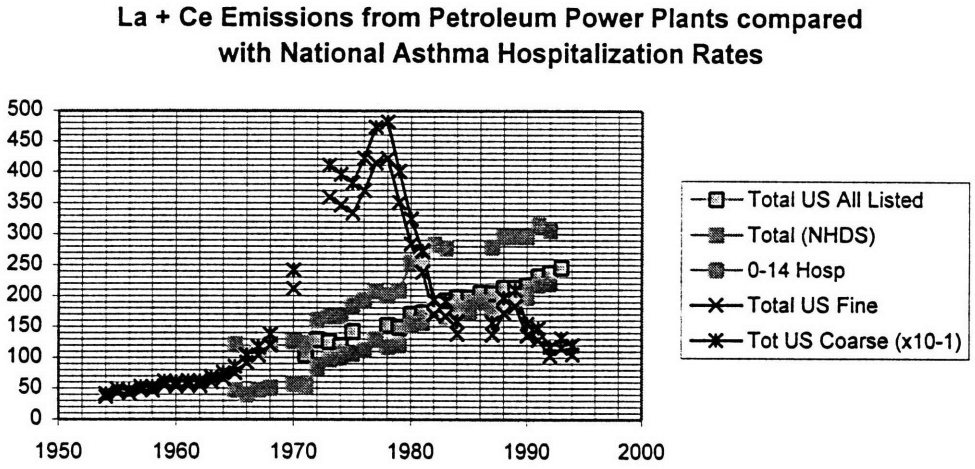


4.1.2 Emissions from Oil-fired power Plants

4.1.2.1 Lanthanide Emissions as Gaged by Power Produced from Fuel Oil

Figure 6 below shows the relative amounts of total La + Ce fine and coarse particle emissions from oil-fired power plants, as measured by the amount of energy produced from fuel oil (section 3.2.2.1), along with national estimates of adult and childhood asthma hospitalization rates. Estimates prior to 1965 are shown, though they are not relevant since lanthanides were not used before the mid-1960s. Both lanthanide emissions and asthma hospitalizations show an increase until about 1978, after which there is a drastic reduction in this measure of lanthanide emissions, while the three measures of asthma rates continue to rise. Hence there does not appear to be a correlation between the two factors, unless the lanthanide emissions remain above the threshold required to cause asthma even when they drop.

Figure 6: Comparison between Emissions and Discharges



Graphs of lanthanide emissions versus hospitalization rates can be generated to evaluate whether there is a causal relationship. Only a poor linear fit can be generated to 0-14 hospitalizations and to total hospitalizations, and even these lines have negative slopes (-0.06 and -0.06 for fine, -0.005 and -0.006 for coarse, respectively). The fit is better for all listed diagnoses, though the slope is even more negative (-0.34 for fine, -0.03 for coarse). Thus there is further indication that lanthanide emissions from oil-fired power plants do not cause increased asthma rates.

Figure 7: Emissions and Discharges Comparisons

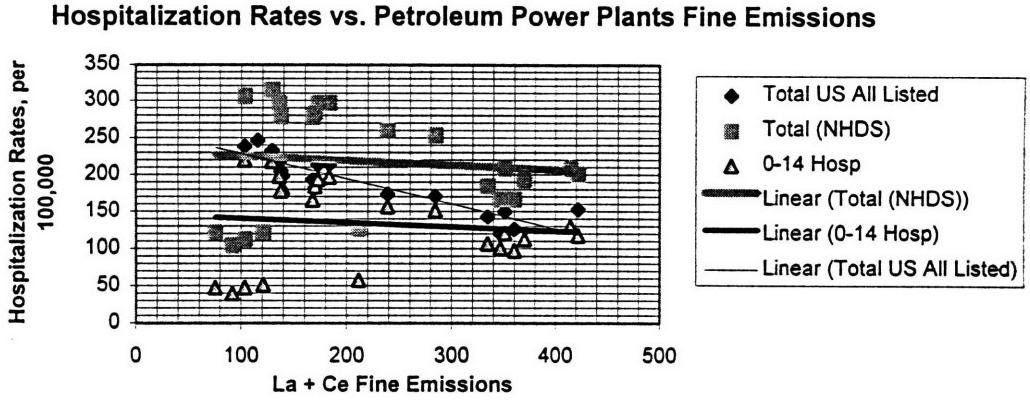
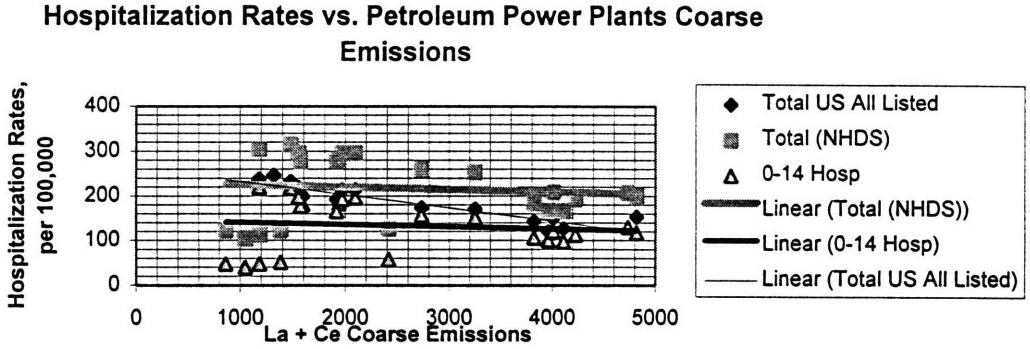


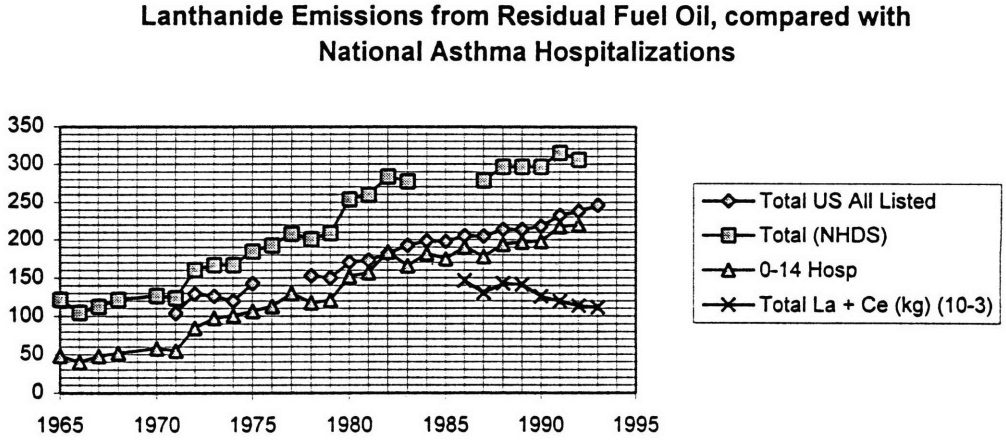
Figure 8: Emissions and Discharges Comparisons



4.1.2.2 Lanthanide Emissions as Estimated from Lanthanide Concentrations in Petroleum

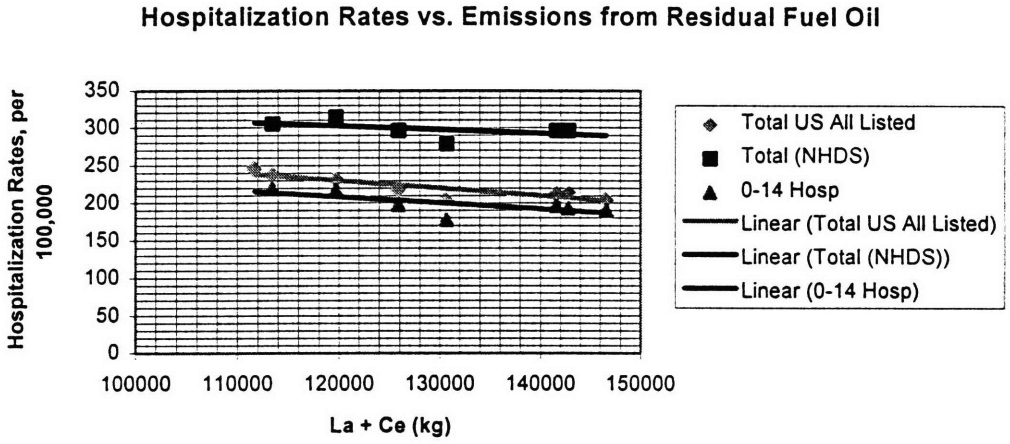
Lanthanum and cerium emissions from total United States consumption of residual fuel oil appears to be relatively constant, or perhaps slightly decreasing, during 1986-1994, as shown below. Since asthma rates are increasing during this time period, a causal relationship could not exist unless emission levels are remaining above a minimal asthma inducing threshold. This latter possibility is not unlikely, given the very large amounts of lanthanum and cerium calculated to be emitted from fuel oil each year.

Figure 9: Residual Fuel Oil and Discharge Comparison



Linear regression of hospitalization rates versus lanthanide emissions from residual fuel oil further suggest a lack of correlation between the two factors. Though the slopes generated from these fits are not significantly negative (total all listed diagnoses: -0.001, total hospitalizations: -0.00049, childhood hospitalizations: -0.00081), and the lines may be horizontal, the data still indicates that a positive correlation cannot be seen.

Figure 10: Residual Fuel Oil Emissions and Discharge Comparisons



4.1.3 Emissions due to Motor Vehicle Usage

Relative fine and coarse lanthanum emissions from motor vehicles are estimated to remain constant between 1981 - 1994, based on the amount of motor vehicle usage as gaged by motor gasoline consumption in a given area. The order of decreasing emissions is South, Midwest, West, and Northeast. This order, however, does not correlate with the relative order of regional asthma rates according to the previoulsy described all listed diagnoses.

4.2 Regional Trends in Lanthanide Emissions and Asthma Hospitalization Rates

4.2.1 Emissions from Oil-fired Power Plants

4.2.1.1 Percent of Power Generated by Oil, Coal and Gas in Regional Divisions

An analysis of each state and region has been shown in the table below, using the percent of power generated by fuel oil and of that generated by coal and gas in each state. States/regions under a strong influence of oil-fired power plants are highlighted, while those with a less definite influence are underlined. If a causal relationship does exist between lanthanide emissions and asthma prevalence, the distribution of states into four regions would give high asthma prevalence rates for the Northeast since most of the states within that region are under the influence of oil-

fired power plants; low rates for the Midwest since most of the states within that region are not under the influence of oil-fired power plants; and mixed rates for the South and West since these regions consist of a mixture of states either under or not under the influence of oil-fired power plants. As would be predicted by such a causal relationship, the Northeast proves to have high rates of all listed asthma diagnoses; however, rates for other regions are not in agreement with those expected in the case of a correlation, since the Midwest appears to have the 2nd highest rates beginning in the late 1980s, and the South and West the lowest.

Table 14: Coal and Gas versus Oil Regional Characteristics

1984 - 1994 Average	% Power Generated by Coal and Gas	% Power Generated by Fuel Oil			% Power Generated by Coal and Gas	% Power Generated by Fuel Oil
Northeast				*Midwest*		
Maine	0.00	19.92		Ohio	91.29	0.54
New Hampshire	35.34	23.04		Indiana	99.10	0.39
Vermont	0.72	1.48		Illinois	46.27	0.71
Massachusetts	44.32	41.59		Michigan	75.69	0.92
Rhode Island	44.92	53.43		Wisconsin	71.01	0.23
Connecticut	7.58	31.63		Minnesota	66.01	0.87
New York	33.97	22.96		Iowa	85.17	0.32
New Jersey	32.54	8.88		Missouri	83.46	0.30
Pennsylvania	65.10	4.10		North Dakota	92.77	0.24
NE Ave	**29.39**	**23.11**		South Dakota	35.60	0.12
				Nebraska	59.26	0.17
South				Kansas	79.36	0.26
Delaware	74.83	25.17		MidW Ave	**73.75**	**0.56**
Maryland	62.68	9.72				
D.C.	0.00	100.00		*West*		
Virginia	49.00	5.03		Montana	59.48	0.11
West Virginia	99.17	0.31		Idaho	0.00	0.00
North Carolina	60.66	0.23		Wyoming	97.70	0.16
South Carolina	35.78	0.12		Colorado	93.89	0.08
Georgia	71.56	0.18		New Mexico	99.14	0.12
Florida	59.47	21.49		Arizona	56.90	0.29
Kentucky	95.12	0.18		Utah	96.31	0.18
Tennessee	72.49	0.24		Nevada	86.31	1.39
Alabama	68.02	0.10		Washington	9.78	0.01
Mississippi	63.79	3.69		Oregon	6.74	0.03
Arkansas	59.07	0.19		California	43.22	2.72
Louisiana	78.69	0.78		Alaska	68.32	9.26
Oklahoma	93.99	0.16		Hawaii	0.00	99.59
Texas	93.59	0.28		W Ave	**55.22**	**8.76**
South Ave	**66.93**	**9.87**				
Total US	**65.99**	**4.30**				

4.2.1.2 Estimates based on Power Generated from Fuel Oil

Calculated relative amounts of fine and coarse particulate lanthanum and cerium from oil-fired power plants emitted over the four regions are shown along with regional all listed hospitalization rates in the graphs below. Trends are the same for both fine and coarse emissions, since identical power estimates were used to calculate both. Though there is a small positive slope for lanthanide emissions in the Northeast, South and West until the mid 1970s, all three show a decrease after the late 1970s. The emission trend for the Northeast decreases until the 1990s, opposite to the increasing asthma trend in the Northeast. This occurs because the total electric utility industry generation by fuel oil decreases in the Northeast between 1990 and 1995 from 4.7 kwhrs/yr to 3.5 kwhrs/yr. The negative slopes of these trends would be even more pronounced if the change in the concentrations of lanthanides used in cracking catalysts had been accounted for. Both emissions and asthma hospitalization rates eventually level off to some extent for the remaining three regions. The dichotomy in the Northeastern trends, however, strongly suggests a lack of correlation, unless the lanthanide emisions in the mid 1970s caused the later trends in asthma rates.

Figure 11: Oil-fired Power Plant Emissions

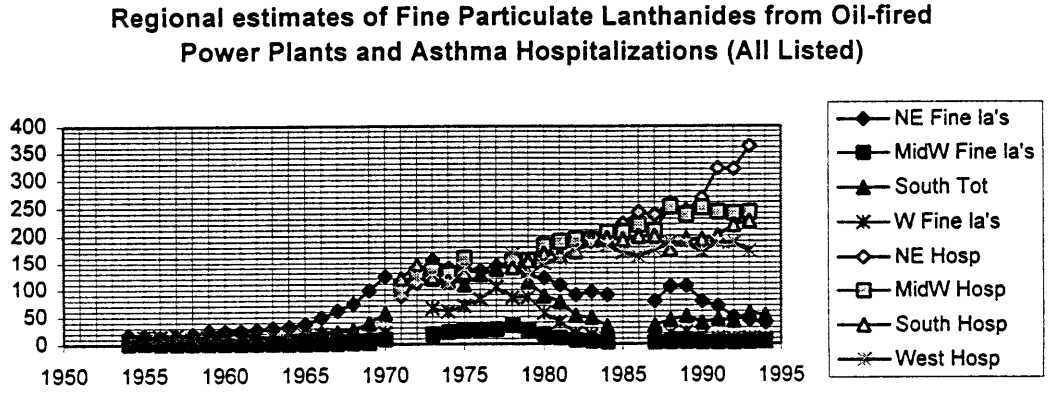
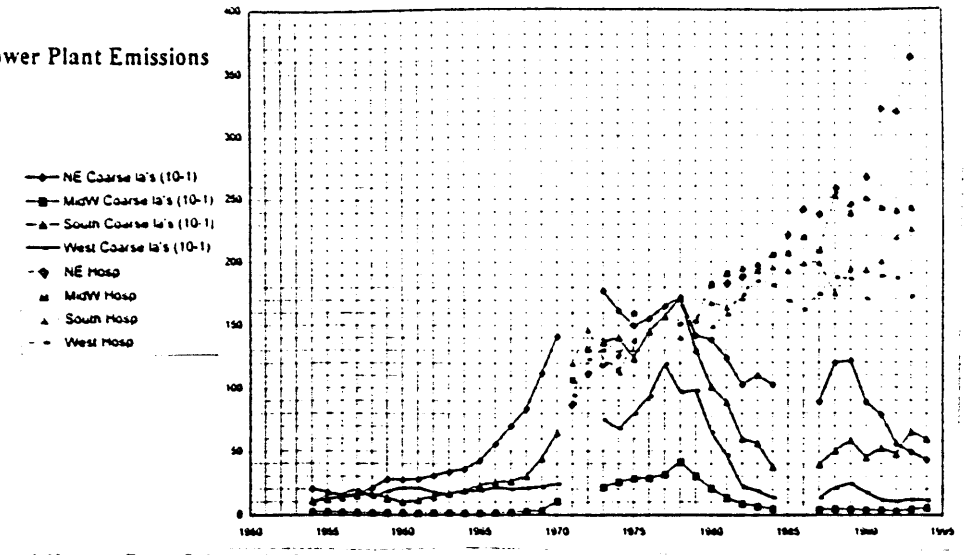


Figure 12: Oil-Fired Power Plant Emissions



Relatively good linear fits of the relationship between regional all listed diagnoses rates versus lanthanide emissions from oil-fired power plants can be obtained and are shown in figures 13 and 14 below. Slopes for all lines are negative, as can be seen in Table 15, further suggesting a lack of correlation. Particularly discouraging is the very negative slope in the Northeast, despite the rising asthma diagnoses in that region.

Figure 13: Linear Regressions for Fine Particulates

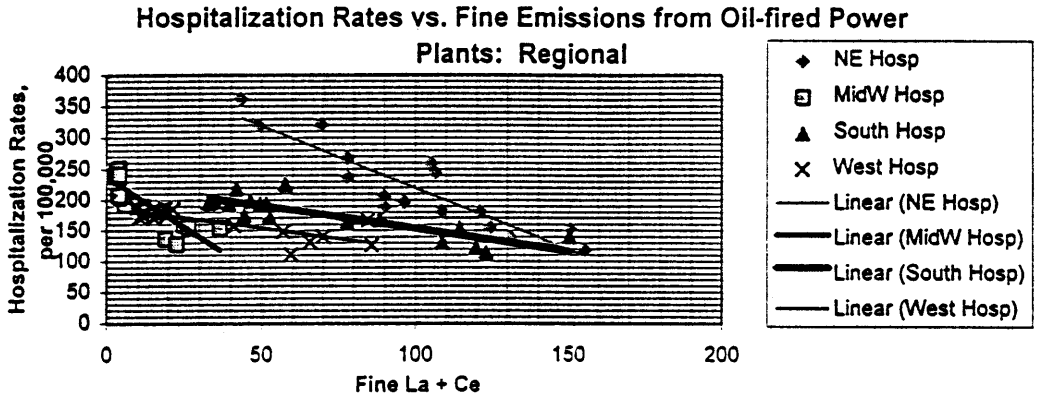


Figure 14: Linear Regression for Coarse Particulates

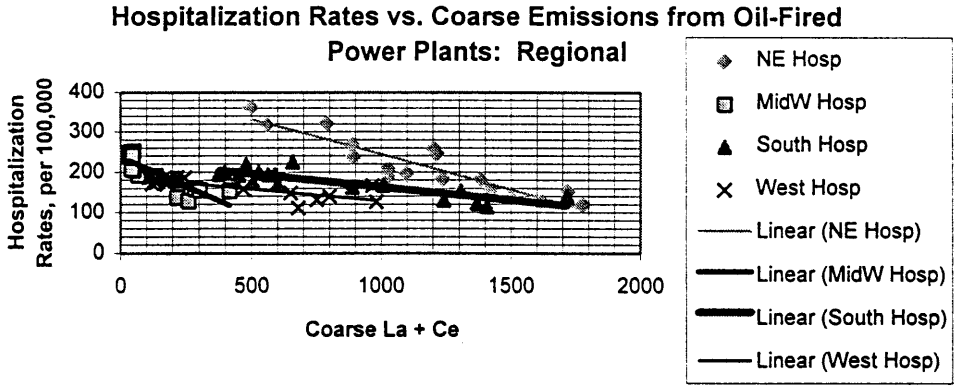


Table 15: Asthma Diagnoses versus Oil-Fired Power Plant Emissions

	Slopes of Diagnoses Rates vs. Fine Emissions	Slopes of Diagnoses Rates vs. Coarse Emissions
Northeast	-2.00	-0.17
Midwest	-3.29	-0.29
South	-0.74	-0.06
West	-0.68	-0.06

4.2.1.2 Estimated Lanthanide Emissions from Petroleum

In 1986 - 1994, leveling off of all listed asthma diagnoses in the Midwest, South and West, though there are large decreases in Northeastern and Western lanthanide emissions as esimated from the concentration of lanthanides in residual fuel oils.

Figure 15: Lanthanide Emissions from Motor Vehicles

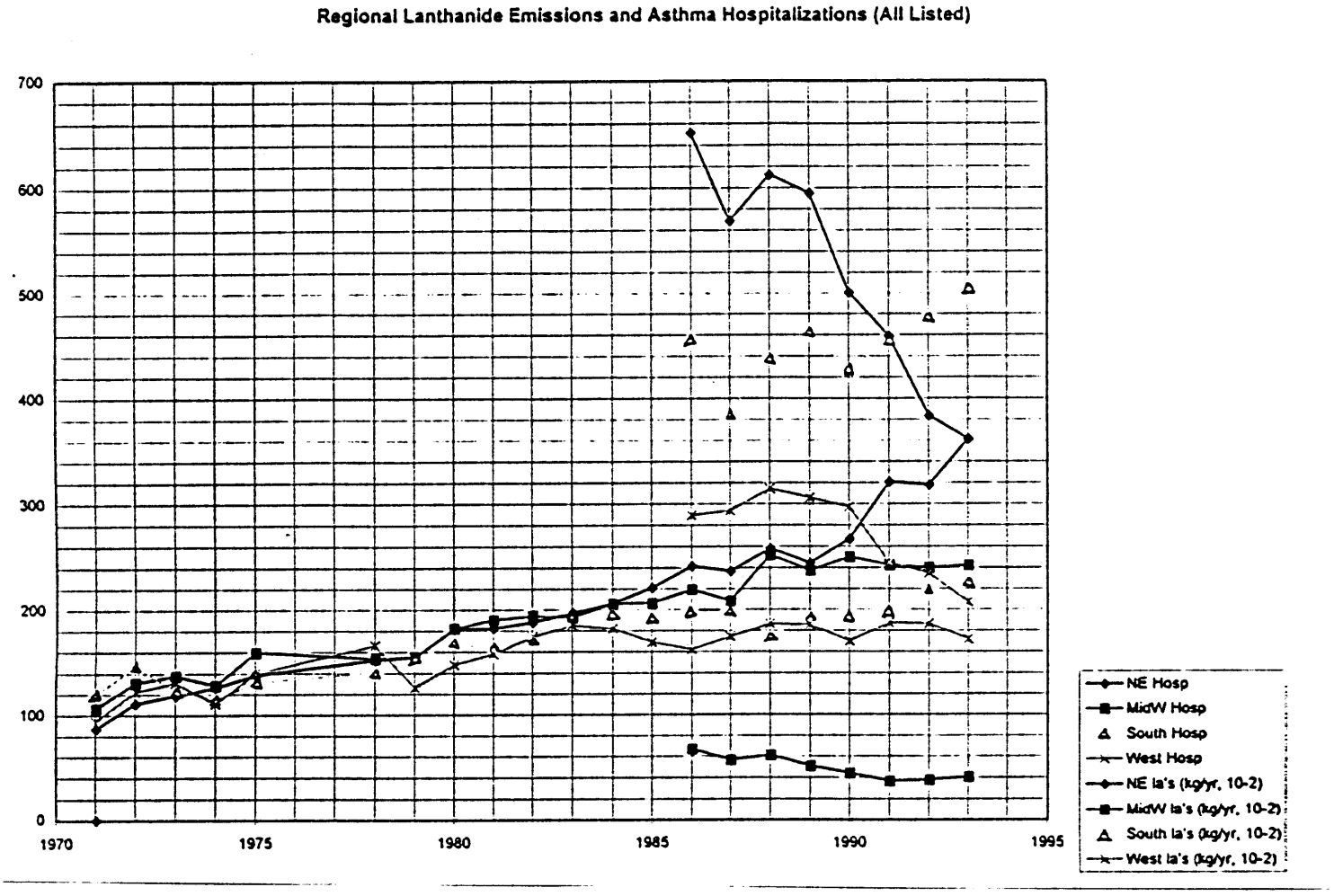
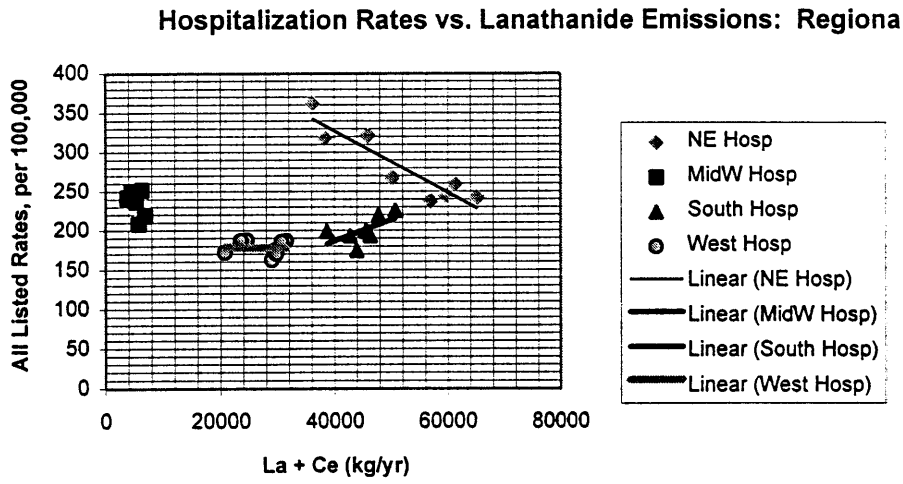


Figure 16: Linear Regressions



4.3 Relative Regional Estimates of Asthma Rates and Lanthanide Emissions

The relative amounts of lanthanide emissions from the various sources considered in Chapter 3 for the four regions of the United States can be compared with the relative rates of asthma hospitalizations in these regions. Such ratios are shown in Tables 16 and 17, below.

Table 16: Asthma Diagnoses Ratios

	All Listed Diagnoses Rates for Asthma		First Listed Diagnoses Rates for Asthma		All Listed Asthma Diagnoses		First Listed Asthma Diagnoses	
	71-80	81-93	68-80	81-93	71-80	81-93	68-80	81-93
NE	1	1.4	1.1	1.3	1.3	1.4	1.4	1.4
MidW	1.1	1.2	1.1	1.2	1.7	1.5	1.6	1.5
South	1	1.1	1	1.1	1.9	1.8	1.8	1.9
West	1	1	1	1	1	1	1	1
Total US	1	1.2	1	1.2	5.9	5.8	5.8	5.8

Estimates of asthma diagnoses do not differ greatly between the four regions of the United States. The significant increase in Northeastern all listed diagnoses rates is not clearly reflected by these ratios. However, though the differences are small, the ratios do reflect slight differences in trends: the Northeast is significantly above average in all listed diagnoses rates, while the West is below average. The ratios of all listed diagnoses are in the following decreasing order: South, Midwest, Northeast, and West.

Table 17: Lanthanide Emissions Ratios

	Fine/Coarse La + Ce from Oil-fired power Plants		% Power Generated by Fuel Oil	La + Ce from Oils Burnt (olmez 9)	Fine/Coarse La from Motor Vehicle Emissions
	68-80	81-94	84-94	86-	81 - 94
NE	6.5	15.9	41.5	10.4	1
MidW	1	1	1	1	1.4
South	5.1	9.7	17.7	9.1	2.2
West	3.1	3.3	15.7	5.5	1.2
Total US	15.7	30.1	7.7	26	5.8

Relative ratios of estimated lanthanide emissions from oil-fired power plant processes (columns 1-3 above) all show the highest emissions in the Northeast, followed by the South, the West, and lastly the Midwest. The significantly higher Northeastern emissions may correlate with the increasing asthma rates in the Northeast. Relative ratios of estimated emissions from motor vehicles (column 4 above) are highest in the South, followed by the Midwest, West, and Northeast.

4.4 Conclusions from Comparisons between Asthma Rates and Lanthanide Emissions

National asthma rate estimates and lanthanide estimates both show increases until the mid 1970s. However, there is little correlation between later trends in asthma rates and lanthanide emissions. Furthermore, though the Northeast is higher than most other regions in many of the estimated regional emissions, limited correlation exists between other regional asthma rate estimates and lanthanide emissions. No where are the significant rises in asthma rates after the 1970s observed in estimates of lanthanide usage. Thus a comparison between national and regional estimates of lanthanide usage and regional asthma hospitalization rates do not suggest a correlation between the two, except for perhaps larger regional trends seen in the Northeast.

4.4.1 Decreased Accuracy of Conclusions due to Established Regional Divisions

The lack of correlation seen in the regional analysis of asthma rates and lanthanide usage may be an artifact of the method in which the country was divided into regions and not to a true absence of correlation. We were constrained to using the regional divisions established by the NHDS, since data was calculated and listed by these regions and not by individual states. However, these regions were determined using geographic considerations and include a mixture of states which predominantly use oil with states which predominantly use coal and gas. The exception to this statement is the Northeast, which happens to consist mostly of oil states. The general mixture of these two categories of states may have diluted an actual correlation between

lanthanide usage and asthma. If the regions separated the states by oil versus coal and gas states, a stronger correlation may have been seen, as in the case of the Northeast.

Chapter 5 Estimates of Lanthanide Depositon in Human Hair

5.1 Collection and Experimental Analysis of Hair Samples

Though lanthanide emissions have been increasing since the 1960s, it remains to be shown that human exposure to these elements has also been increasing. As a source of information on human exposures to environmental pollutants, hair samples were collected from residents of the Woburn, MA area, after a request for them was made at a Woburn public town meeting. Most of the samples came from residents of Woburn, though some were from non-residents within a 50 mile radius from Woburn. Residents of this area would be exposed to lanthanide emissions both from refineries and from motor vehicles. The hair offered was often that saved as memorabilia or for other such purposes, often from the early childhood of the person from whom the hair originated. One-hundred and nine samples were obtained, dating from 1938 - 1994, of which approximately eighty eight were included in the analysis. The concentrations of various elements in the sample were measured using instrumental neutron activation analysis (INAA) under Dr. Ilhan Olmez of the Nuclear Reactor Laboratory, MIT. The original purpose of analyzing these hair samples was to investigate human exposures to arsenic and chromium; however, it proved very useful to extend this analysis to our study of lanthanide exposures. Since concentrations of lanthanum and cerium can be detected in these hair samples, trends in these concentrations might have indicated whether the increase in lanthanide usage is actually leading to increased levels of childhood exposure.[50]

The hair samples were prepared by researchers at the MIT Nuclear Reactor Lab and Center for Environmental Health Studies. Each sample was soaked in 10% nitric acid, washed with de-ionizing water, and then irradiated. After three months, a similar irradiation was conducted for the 96 hair samples whose masses were greater than 1 mg, after they were washed with acetone and then water. These washing procedures were conducted in an attempt to remove all external depositions on the samples, so that only those elements deposited into hair after internalization into the body would be detected.

[50] Catriona, ER, Trowbridge, PR, Hemond, HF, Tomita, A, Chen, J, Thilly, WG, Gone, J and Olmez, I. Historical Exposure to Arsenic and Chromium in the Aberjona Watershed, as Determined by Concentrations in Human Hair.

5.2 Statistical Analysis of Metal Concentrations Detected in Hair Samples

5.2.1 Linear Polynomial Fits

The concentrations of various elements detected in the hair samples were plotted against respective years of sample origination, and first degree polynomial fits to these data were generated, using the analytical tool known as Matlab. If the increase in lanthanide usage has been affecting childhood exposure to lanthanum and cerium, the concentrations of these elements in hair would give a positive slope. To account for the weight of samples from years prior to lanthanide usage, separate slopes were calculated for the separate time periods of interest, with the following results expected as indications of increased exposure. Lanthanide concentrations in hair should increase after the 1960s, since by 1969, lanthanide usage in refineries was widespread, and since after 1981, lanthanide usage in catalytic converters had begun. Thus first degree polynomial fits were calculated separately for the 1938 - 1965 and 1966 - 1994 time periods, and for the 1938 - 1968 and 1969 - 1994 time periods. Cerium exposure should increase after 1981, due to its usage in catalytic converters, though its usage in refineries was not as significant. Hence, separate slopes were also calculated for the 1938 -1979 and 1981 - 1994 time periods. (No samples from 1980 were available.) Samarium and scandium are crustal elements with no known anthropogenic sources, and were used as controls with which to compare the trends in lanthanum and cerium. Results from these polynomial fits are shown in Table 18 below, while actual graphs and fits can be found in Appendix B. Concentrations are in μg element per grams hair, giving slopes in μg/gr per year. Matlab gives slopes correct to four decimal places; hence values such as -0.0000 indicate that though there are no significant digits to four places after the decimal point, the number is not exactly 0, but is rather slightly negative.

Table 18: Slopes for First Degree Polynomial Fits to Hair Data

	1938 - 1994	1938 - 1965	1966 - 1994	1938 - 1968	1969 - 1994	1938 - 1971	1981 - 1994
La	0.0012	-0.0004	0.0008	0.0009	0.0009	0.0020	0.0055
Ce	-0.0164	0.0225	-0.0151	0.0060	-0.0157	-0.0059	0.0119
Sm	0.0000	-0.0001	-0.0000	-0.0000	-0.0000	0.0001	0.0001
Sc	-0.0000	0.0000	-0.0000	-0.0001	-0.0001	0.0000	-0.0001

The results from these polynomial fits give values which are deceptively supportive of increased levels of exposure. As can be seen in the table above, while samarium and scandium concentrations remain constant in all time periods, very slight increases in exposure are detected for lanthanum and cerium exactly when expected. Lanthanide concentrations have a negative

slope before 1966, and yet a positive slope after 1966. Furthermore, lanthanide concentrations have a positive slope until 1971, and an even more positive slope after 1981. Cerium, on the other hand, has a negative slope until 1971, but a positive slope after 1981. However, the actual values of these slopes reveal that the changes noted are insignificant. None of the calculated slopes differ from 0 by more than 0.03 μg/gr. Furthermore, if these values were significant, slopes for cerium prior to 1966 and to 1969 would be positive; however, given that there were no known major anthropogenic sources of cerium prior to 1981, this result could not logically be explained. Thus it appears that no significant increases in exposure to lanthanum or cerium can be detected via analysis of human hair samples.

5.2.2 Concentration Distributions over Time Periods of Interest

Histograms were generated for each of the time periods analyzed above, in order to observe the distribution of concentrations within each time period. Again, time periods in which human exposure was increased would show distributions more heavily weighted towards larger concentrations. The concentration ranges in which the largest numbers of samples fell (range of highest frequency), as well as the concentration range by which 85% or more of the samples had fallen (smallest range with cum % ≥85), are shown in Table 18 below. Listed concentration ranges span all concentrations greater than the given minimum value, up to and including the given maximum value. Concentrations are given in units of μg/gr (ppm), and are rounded to three significant figures. Actual histograms can be found in Appendix C .

Table 19: Hair Histogram Results

	La		Ce		Sm		Sc	
	Range of Highest Freq	Smallest Range with cum % ≥ 85	Range of Highest Freq	Smallest Range with cum % ≥ 85	Range of Highest Freq	Smallest Range with cum % ≥ 85	Range of Highest Freq	Smallest Range with cum % ≥ 85
1938 - 1994	0.002 - 0.085	0.002 - 0.085	0.035 - 1.70	0.035 - 1.70	0.001 - 0.005	0.01 - 0.015	0.000 - 0.002	0.002 - 0.0050
1938 - 1965	0.006 - 0.036	0.036 - 0.067	0.11 - 3.09	0.11 - 3.09	0.001 - 0.01	0.01 - 0.018	0.001 - 0.002	0.004 - 0.005
1966 - 1994	0.002 - 0.109	0.002 - 0.109	0.035 - 0.544	1.05 - 1.56	0.001 - 0.005	0.009 - 0.013	0.000 - 0.003	0.003 - 0.005
1938 - 1968	0.006 - 0.041	0.041 - 0.077	0.11 - 2.59	0.11 - 2.59	0.001 - 0.008	0.008 - 0.015	0.000 - 0.002	0.004 - 0.005
1969 - 1994	0.002 - 0.109	0.002 - 0.109	0.035 - 0.544	0.544 - 1.05	0.001 - 0.005	0.009 - 0.013	0.000 - 0.003	0.003 - 0.006
1938 - 1979	0.002 - 0.083	0.002 - 0.083	0.064 - 2.20	0.064 - 2.20	0.001 - 0.007	0.007 - 0.013	0.000 - 0.003	0.003 - 0.006
1981 -	0.004 -	0.004 -	0.035 -	0.661 -	0.001 -	0.006 -	0.000 -	0.004 -

1994	0.153	0.153	0.348	0.974	0.006	0.012	0.004	0.007

In the case of increased exposures, the concentration ranges for later time periods would be higher than those for earlier time periods. Instead, observed concentration ranges in the different time periods involved are very close and do not show any statistically significant differences. Lanthanide concentration ranges containing the highest frequency of samples span a larger breadth during periods of expected increased emissions, and encompass the ranges of highest frequency during respective periods of lower emisisons. In the case of cerium, the opposite is true: cerium concentration ranges containing the highest frequency of samples span a larger breadth during periods of lower emissions, and include the highest frequency ranges of periods of higher emissions.

As expected, the Sm and Se concentration ranges within which most of the samples fall, and by which 85% cumulative percentage has been reached, are almost exactly the same in the different time periods analyzed, indicating no change in exposure characteristics to these elements over time.

The above values can be more clearly understood upon comparing the averages in the given ranges, as shown in Table 20 below.

Table 20: Averages from Hair Histograms

	La		Ce		Sm		Sc	
	Ave with Highest Freq	Smallest Ave with Cum % ≥ 85	Ave with Highest Freq	Smallest Ave with Cum % ≥ 85	Ave with Highest Freq	Smallest Ave with Cum % ≥ 85	Ave with Highest Freq	Smallest Ave with Cum % ≥ 85
1938 - 1994	0.044	0.044	0.868	0.868	0.003	0.012	0.001	0.004
1938 - 1965	0.021	0.052	1.6	1.6	0.006	0.014	0.002	0.004
1966 - 1994	0.056	0.056	0.29	1.305	0.003	0.011	0.002	0.004
1938 - 1968	0.024	0.059	1.35	1.35	0.004	0.023	0.001	0.004
1969 - 1994	0.056	0.056	0.29	0.797	0.003	0.011	0.002	0.004
1938 - 1979	0.042	0.042	1.13	1.13	0.004	0.01	0.002	0.004
1981 - 1994	0.078	0.078	0.192	0.818	0.004	0.009	0.002	0.006

Some slight increases can be seen in the distribution of lanthanum concentrations from the earlier to later time periods as grouped above. However, the average concentrations at which the samples are concentrated do not differ by more than 0.04 μg/gr. On the other hand, the most common cerium concentrations decrease over the time periods in which they are expected to increase. As previously noted, there are only negligible differences, if any, in the Sm and Sc concentration distributions over the given time periods.

Thus, the distribution of lanthanum or cerium concentrations in hair does not differ significantly between the different time periods analyzed. Such a finding suggests that there is no increase in human exposure to lanthanides in the Woburn area, even though emissions from refineries and motor vehicles would have reached this area..

5.3 Conclusions from Studies of Hair Samples

Analysis of concentrations of lanthanum and cerium in human hair do not reflect increased levels of exposure to lanthanides, when analyzed using first degree polynomial fits of concentrations over time, or when analyzed using histograms of concentration distributions during the time periods of interest. Thus, children in the Woburn area do not appear to be experiencing increased levels of exposure to lanthanides, even if lanthanide emissions are increasing in this area. These findings can reflect one of four possible situations:

1) A causal relationship between lanthanide emissions and childhood asthma cannot exist, since there is no increase in actual lanthanides inhaled by children even when emissions rise;

2) Exposure to lanthanides leads to limited deposition in human hair, the threshold of which has already been reached in our samples. Increased intake of lanthanides thus cannot be observed in hair, but could be observed in other parts of the body;

3) Other factors in Woburn, such as wind patterns and vegetation, limit childhood exposure to lanthanides in that particular region; or

4) The detection techniques used allow for limited detection of lanthanides in human hair. This explanation seems unlikely, however, since a wide range of concentrations were able to be detected, suggesting that a significant increase in exposure would have been observable.

Hence, further investigations need to be done in order to determine why no increase in deposition of lanthanum or cerium in human hair have been observed. The biodistribution of inhaled lanthanides needs to be understood, and whether or not significant concentrations of lanthanides can deposit in human hair remains to be established. Similar hair studies in other

communities could also be conducted in order to further understand and validate these findings in Woburn.

Chapter 6: Experimental Measures of Environmental Deposition of Lanthanides

Though measures of lanthanide emissions have been estimated, environmental studies need to be conducted in order to evaluate the actual amount of lanthanides which collect in a given area. Dirt samples from ponds and lakes, or from wetlands and peet, can be analyzed using INAA in an attempt to gage exposure to atmospheric pollutants in a given area. The depth of such samples can serve as approximate time lines over which to evaluate historical exposures.

6.1 Experimental Analysis of Sediment Cores

Analysis of four sediment cores were attempted. The procedures used to obtain, prepare, and analyze these cores were not clearly established before our work began, and so were slowly developed as our experience grew.

6.1.1 Methods of Obtaining Cores

All sediment cores were obtained using Department of Environmental Engineering Professor Harry Hemond's steel corer. Approximately 4 1/2 feet tall, the corer can be divided into two portions. The top half is a hollow cylinder and opens into the bottom half, which is a hollow half-cylinder ending in a pointed end. The general procedure of obtaining a sediment core involves lodging the corer into the sediment at the bottom of the pond or lake; this often required forcing the corer down, sometimes by banging the top with a large rock. After dropping small pieces of dry ice into the corer from the top hole, methanol is added to create an evenly distributed cold temperature. The corer is then capped and sediment is allowed to freeze onto the flat portion of the bottom half of the corer. A one or two inch layer of sediment usually did not take greater than 5 to 10 minutes to freeze onto the corer. The corer is then pulled up, and the frozen sediment core is wrapped in polyethylene (Saran Wrap, for example) and kept in a cooler or freezer.

Due to a misunderstanding of the instructions in using the corer, the flat portion of the corer was lubricated at the beginning. This made the surface slippery, and could cause the frozen core to drop back into the water as the corer was lifted out of the sediment. This could have led to mixing or contamination of the cores for which this occurred.

In May 1996, three cores were obtained from Fulton County, New York by Michael Ames and Charu Puri; 2 from Hale Creek, and 1 from Vandenburg Pond. Hale Creek is a small, marshy roadside pond, probably not with any recreational use. The cores were about 20 cm, the first one having a lumpy layer on its surface which was somewhat haphazardly wiped and which could have led to mixing of the layers. The second one fell into the water while frozen, but was caught. Vandenburg Pond, where the third core was collected, is a cleaner, larger, pond, apparently used recreationally at least for swimming. The pond surface had a sandy top layer, followed by more organic matter.

In August 1996, Jec Gone, Ames, and Puri obtained two cores from Western Massachusetts. The first was obtained from Horn Pond, in Woburn. This pond was used for some recreation, for we observed children fishing. The second core was obtained from Lake Quannapowitt in Wakefield. Located near a decent sized road, this lake was often used recreationally, even for boating, and had a very very rocky sediment into which the corer was pushed with exceptional difficulty.

6.1.2 General Preparation of Cores

The following is the order in which our sediment cores were analyzed: the second core obtained from Hale Pond (Hale2), the first core obtained from Hale Pond (Hale1), the core obtained from Lake Quannapowit (LakeQ) and the core obtained from Horn Pond (Horn). The learning curve in sample preparation was tremendous, and techniques were modified with experience.

Shortly after it was obtained, each core was cut along its length into approximately 1 centimeter pieces, on a marble slab placed in an unused hood across from the freezer in which the cores were stored. At first a hot wire also lent to us by Professor Hemond's laboratory was used to attempt to cut through the frozen core. However, the wire was not very strong, had to be changed, and took too long time to melt the sediment, so that other portions of the core also began to melt. A stainless steel bread knife was used in conjunction with this hot wire, and eventually the hot wire was discarded in preference for the bread knife alone. The following procedure is used in actually cutting the cores: the marble slab is cleaned with methanol and then with de-ionized water, and the core is then removed from the freezer and placed on the marble slab. A few portions are cut from the core and placed into separate labeled clean bags, washing the bread knife with de-ionized water in between cutting each portion. The remainder of the core is then refrozen by placing it back into the freezer for a few minutes, the labeled bags are put into

the freezer, and the marbles slab is again wiped. The refrozen core is then placed on the marble slab again, and a few more portions are cut. Thus the entire core is cut into 1 cm pieces, each stored in individual plastic bags. These bags are then placed together into larger plastic bags, so that the entire core is stored in the freezer in two larger bags.

6.1.3 Preparation of Cores for INAA

Cores were prepared for INAA using the following general procedure. Three to four types of samples were prepared for each depth analyzed. Due to the gradual development of preparation techniques with experience, some of the steps do not apply to all cores, as specified below.

1) Empty centrifuge tubes and inside/outside clean bags are weighed on a balance in the hood in the Olmez clean laboratory in building NW12 at MIT. Clean bag and vial preparation are described below.

2) For each centimeter to be analyzed, a very small portion of sediment is cut and placed in an inside/outside clean bag in a labeled cleaned vial, and a larger portion of sediment is placed in a labeled centrifuge tube. This is done for a few portions at a time, in the unused hood across from the freezer on the cleaned marble slab. The samples are allowed to defrost for a few hours under the hood in the clean laboratory. The small portion of sediment is left untouched and will give the "sediment as is" samples.

3) The samples in the centrifuge tubes are centrifuged using the centriguge in the Olmez hot laboratory in NW12, for 10 - 15 minutes. In the case of some cores, samples were centrifuged after soaking in de-ionized water for at least one hour, with occasional mixing. For some cores, a teflon filter is then rinsed with deionized water. The pore water separated during centrifugation is syringed through the filter and collected in an inside/outside clean bag placed in a clean vial, giving the sample known as "pore water."

4) 10% nitric acid is added to the remaining sediment in the centrifuge tubes, allowing the sediment to be leached by the acid for at least one hour, mixing occasionally. The samples are again centrifuged for 10 -15 minutes, syringed through a rinsed teflon filter for some cores, and collected in inside/outside cleaned bags placed in clean vials, to give "acid leachate" samples.

5) After the masses of all samples + bags is taken on the same balance used above, the samples are kept in vials in a dessicator, and frozen at least overnight. The samples are then freeze dried until all moisture seems to have been removed, which generally took a few days.

6) Samples are again weighed on the same balance. Bags are sealed and placed in labeled outside cleaned bags. In the case of the sediment as is, a small portion of the freeze dried sediment is placed in a new inside/outside cleaned bag, which is then packaged in a labeled outside cleaned bag.

7) Samples are then put in rabbits, and sent for irradiation.

8) Metal concentrations are then detected using four detectors in the Olmez counting lab in NW12.

Inside/outside clean bags were prepared by cutting polyethylene strips into appropriately sized pieces and sealing them at one end in order to make a bag. All bags were soaked first in nitric acid, and then in de-ionized water; bags were then dried for in the hood in the Olmez clean laboratory. Outside clean bags were prepared just by cutting and sealing the same polyethylene bags used above. Plastic vials were cleaned by soaking in water and nitric acid, rinsing with deionized water, and then drying in the same hood.

6.1.4 Hale2

Hale2 was only analyzed at four depths: 2 cm, 7 cm, 12 cm, and 17 cm, in the attempt to observe an overall depth profile of the core. The as is and acid leachate samples were prepared as described above. 1.7 - 2.5 ml of leachate was collected. No deionized water was added to the samples, however, so only approximately 1.5 ml pore water could be collected after centrifugation. In addition to these three samples, a small portion of the sediment remaining after the collection of pore water and leachate was analyzed as "remaining" samples. The samples were accidentally connected to the freeze drier before they were frozen, and the resulting vaccuum pressure caused some of the water and leachate samples to splash in the desicator. Splashing into the vials of other samples appeared to have been minimum, so we assumed that this did not cause excessive contamination of other samples. Two blanks were analyzed along with the samples: blank1 was just a plain inside/outside cleaned bag, and blank2 was an inside/outside cleaned bag with approximately 2.5 ml 10% nitric acid. None of the samples were filtered, since it was not clear that filtration would be necessary.

Samples were leached in an attempt to collect extractions from the sediment. The chemical processes involved in leaching sediment with nitric acid are complicated, however, and so it is unclear as to whether the "leachate" samples give accurate or valid results for this or other cores taken. The "remaining" samples did not appear to give clear information, and so were not collected for any other cores.

6.1.5 Hale1

Hale1 was analyzed at every other centimeter, from the top of the core (the 1 cm portion) to the bottom of the core (the 23 cm portion). Only "as is" and "pore water" samples were prepared and analyzed. An empty inside/outside cleaned bag served as the only blank, labeled as blank1. The "pore water" sample at 13 cm spilled outside of its bag, and so was pipetted from its hopefully clean vial into a new inside/outside cleaned bag. Samples were still not filtered.

6.1.6 LakeQ

LakeQ was also analyzed at every other centimeter, from the top of the core (1cm) to the bottom of the core (21cm). The core proved to be too rocky to give any pore water after defrosting, and so sediment was leached in order to give another category of samples in addition to the "as is" samples. Unfortunately, however, this second category cannot be compared with the second category in Hale1. Three blanks were analyzed with the samples; blank1 was an empty inside/outside cleaned bag, blank2 was an inside/outside cleaned bag with approximately 5ml deionized water, and blank3 was an inside/outside cleaned bag with approximately 5ml dilute acid. Blank2 was not used in calculating sample concentrations. Since this lake does not appear to be in a particularly polluted region, it may reflect background levels of natural and anthropogenic metals in the atmosphere.

6.1.7 Horn Pond

Horn Pond was also analyzed at every other centimeter, from portions at 1 to 23 cm along the core. Along with "as is" samples, samples were analyzed after leaching with approximately 5 ml acid and after leaching with approximately 4 ml water, since pore water alone could again not be obtained. Three blanks were again analyzed with the samples: blank1 an empty inside/outside cleaned bag, blank2 an inside/outside cleaned bag with approximately 3ml deionized water, and blank3 an inside/outside cleaned bag with approximately 4.5ml dilute acid. Horn Pond is in the Woburn Superfund Site, though it does not appear to be fed by the Aberjona River. Thus, unlike sediment from LakeQ, analysis of Horn Pond samples should refledt high levels of contamination.

6.2 Analysis of Sediment Core Data

Analysis of data from INAA of sediment cores is done in three steps:

1) Subtraction of concentrations detected in blank bags from those detected in samples.

2) Calculation of enrichment factors. Enrichment factors allow one to estimate the relative amount of metals contributed from anthropogenic sources. Scandium concentrations were used to normalize other metal concentrations, since the only major source of scandium is in the crustal material of the earth. Standard crustal concentrations were taken from Taylor's crustal abundances. Enrichment factors were calculated according to the following equation: $EF_{La/Sc} = ([La]_{sample}/[Sc]_{sample}) / ([La]_{crustal}/[Sm]_{crustal})$.

3) Calculation of lanthanum/metal ratios: Ratios of lanthanum concentrations to other metal concentrations were also calculated.

Increasing trends in lanthanum or cerium enrichment factors, or in lanthanum/other metal ratios, with decreasing depth would suggest an increase in exposure to lanthanum or cerium over time. Though observed La/Ce ratios were relatively constant, indicating that these two metals are used similarly, little other conclusive trends could be seen in this data.

6.3 Conclusions from Sediment Analysis

Results from analysis of sediment cores do not show any distinct trends, increasing, constant or rising. These results could be due to one or a combination of several factors listed below.

1) Specific sample preparation procedures or tools employed may not have been appropriate for accurate and consistent detection of lanthanides by INAA, since it is known that INAA can detect lanthanide concentrations in other experiments. For example, it is possible that the cores we were able to take in our studies did not extend deep enough to allow a rise in lanthanide concentrations to be observed. Sediment from San Pedro, California, for example, in which increased lanthanide concentrations were observed, reached 36 cm in depth, and showed an increased only in the top 20 cm.[51]

2) Sediment may not be the most ideal medium in which to measure lanthanide concentrations using INAA. We do not know how the physical and chemical processes of lanthanides in sediment, and are not sure if they are collected at certain depths or densities. Furthermore, sediment samples inherently have higher levels of crustal matter and background dirt levels, which can make small changes in anthropogenic metals more difficult to detect. Though increases in lanthanide concentrations have been observed using INAA in samples from sediment

[51] Olmez, I, Sholkovitz, ER, Hermann, D and Eganhouse, RP. Rare Earth Elements in Sediments off Southern California: A New Anthropogenic Indicator. Environmental Science Technology. 25:2, 1991, 310 - 316.

directly under refinery influence, it is possible that more indirect contributions/ sources cannot be observed at a distance in sediment.

Thus, conclusive information from our sediment core analysis was not obtained.

6.4 Analysis of Wetland Cores

Wetlands may prove to be more appropriate media for measuring lanthanide deposition for three major reasons: 1) organic matter in wetlands provides natural filtering and binding activities which could trap environmental pollutants in place, 2) decreased relative amounts of dirt in wetlands allows for lower background levels of crustal and other elements than in sediment, and 3) deeper cores can more easily be obtained from wetlands. In 1991, a wetland core from McQuesten Brook in Manchester, New Hampshire had been taken by Ronald H. Miller's biology class at the West High School (Manchester, New Hampshire). This wetland lies in an urban setting, near an auto garage, and was analyzed for various elements at the MIT Nuclear Reactor Laboratory, using INAA. Data from this wetland core are analyzed below.

6.4.1 Analysis of Wetland Data

Retrospective analysis of data obtained from this wetland core allows us to trace lanthanide deposition in this wetland. The results significantly suggest a rise in exposure levels to lanthanides, revealing increases in lanthanum, and, to some extent, cerium and neodymium concentrations, as can be seen in Figures 17 and 18 shown below. This increase could be explained by increased emissions due to area petroleum refineries or to motor vehicle usage.

Unfortunately, the validity of these findings is slightly questionable, since this core had only been analyzed at four depths: 0 - 5 cm, 5 - 10 cm, 10 - 15 cm, and 65 - 70 cm. Decreased concentrations are only seen for the lowest point, and could potentially be due to an experimental error when handling that sample. Furthermore, all of the physical interactions between wetlands and lanthanides are not fully understood. For example, lanthanide deposition may actually have occurred consistently over time with no increase, but have been slowly sifted and collected towards the bottom of this wetland. This process would give the same results as those observed in our analysis.

Figure 17: Wetland Core Enrichment Factors

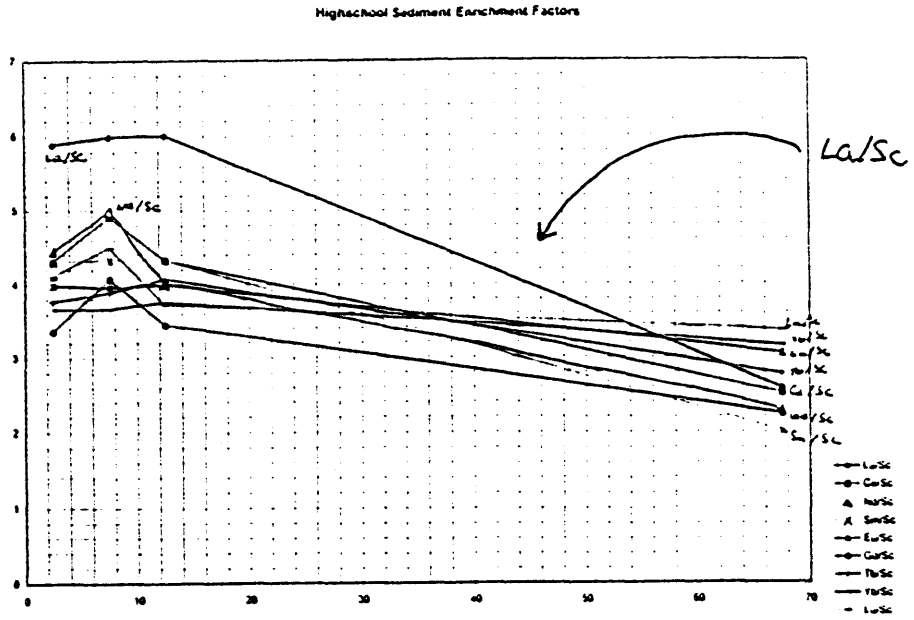
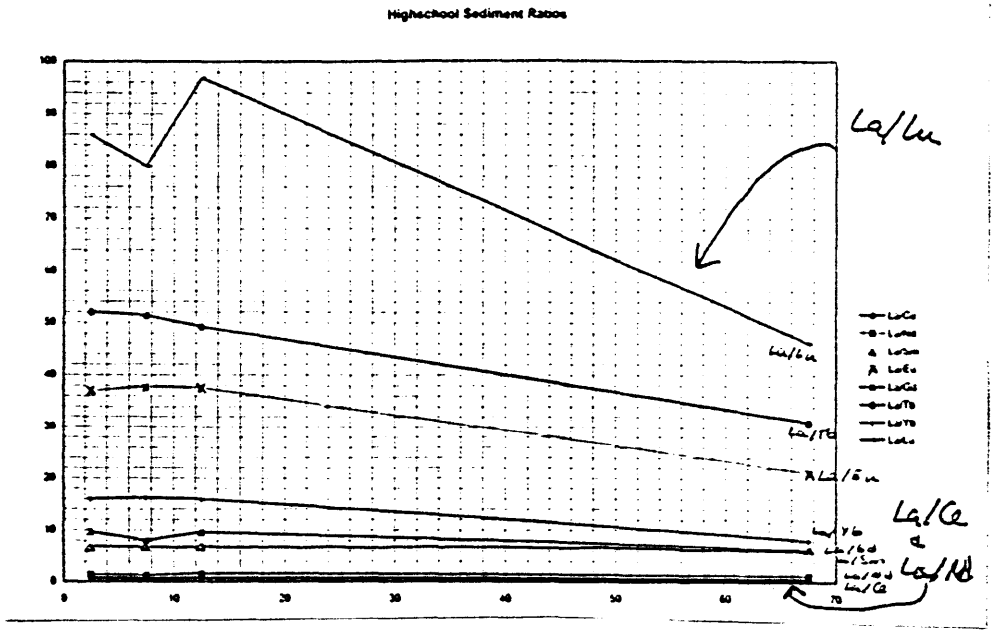


Figure 18: Wetland Core Lanthanum/Metal Ratios



6.4.2 Conclusions from Analysis of Wetland Data

From the above discussions, it is evident that further investigations of wetland cores using INAA must be conducted in order to fully understand deposition of lanthanides in such cores. Perhaps such investigations will consistently show increasing lanthanide concentrations,suggesting a rise in human exposure to these metals.

Chapter 7 Conceivable Roles of Lanthanides in Asthmatic Reactions

7.1 Pathology of Asthma

Asthma is caused by chronic inflammation which leads to airway hypersensitivity and bronchoconstriction. The disorder can be thought of as progressing in three stages: an early-phase reaction - with an emphasis on bronchoconstriction, a late-phase reaction - with an emphasis on bronchial hyperreactivity and edema, and then ongoing chronic processes including bronchial hyperreactivity, epithelial damage, and mucous hypersecretion. Mast cells serve as the most important effector cell in the early-phase. Other cells which may play a role in early-phase reactions include macrophages and platelets. Mediators such as platelet activating factor (PAF) and LTB4 from mast cells and lymphokines from T cells attract and activate eosinophils, neutrophils, and macrophages, leading to late-phase reactions. Accumulation of these cells and mediators leads to a chronic state of inflammation.[52]

The onset of asthma can occur due to both allergic and non-allergic stimuli, due to nervous system changes, or due to the exposure of susceptible bronchial airways to infections. Thus specific or nonspecific immune responses and hyperreactivity can induce asthmatic reactions. Thereafter, asthmatic processes may proceed in immunoglobulin E (IgE) antibody-independent pathways and/or IgE-dependent pathways. The physiological processes and clinical symptoms observed in asthmatic reactions are dictated by multiple processes at the molecular level. Since one likely mechanism by which lanthanides could induce asthmatic reactions relates to an allergic response, some of the processes involved in allergic asthma and, to some extent, in some forms of non-allergic asthma are discussed below. These processes can be outlined as follows:

1) Initial exposure to allergen.
2) Sensitization of tissue to allergen via IgE antibodies.
3) Reexposure to allergen.
4) IgE mediated response to allergen.

Inhaled allergens are injested by accesory cells in the lung, which digest the allergen and present it via MHC II molecules. CD4+ T cells are equipped to recognize foreign substances bound to these MHC II molecules. Thus those CD4 + T cells with T cell receptors specific for the antigen-MHC II complex generated will be activated by these antigen presenting cells, and develop into clones of Th2 cells (Thelper 2). Via CD40 - CD40 L-ligand interactions and the release of cytokine interleukin 4 (IL-4), these Th2 cells induce B lymphocytes to switch from

[52] Kay, AB. Leucocytes in Asthma. Immunological Investigations. 17: 8 & 9, 1988, 679 - 705.

production of IgG and IgM antibodies to IgE antibodies specific for the allergen exposed to. Basophils and mast cells may also induce the production of IgE antibodies via CD40 and IL-4 based mechanisms. Trans-membrane receptors on effector cells such as basophils, mast cells, platelets, macrophages and possibly Langerhans' cells and eosinophils, bind the constant portion of these antibodies and are thus "sensitized" to the specific allergen recognized by these antibodies. These T cells can also induce leukocyte influx directly after exposure to antigen. Reexposure to the initial allergen then allows this allergen to bind and cross-link IgE molecules on effector cells, and thus to activate these cells to release inflammatory mediators. These mediators go on to effect other cells, and cause such processes as inflammation and other symptoms of disease. Inflamation of the airways occurs due to an upregulation of endothelial adhesion molecules and their respective activated leukocyte ligands, which recruits inflammatory cells from circulation.[53,54,55,56]

A lung can be sensitized to one or many specific allergens by the process outlined above. This sensitization could then allow increased hyperresponsiveness to other antagonists in the environment, furthering the asthmatic symptoms experienced.

The increased likelihood in some individuals to develop IgE mediated immediate hypersensitivity reactions when encountering allergens found commonly in the environment is referred to as atopy. Atopic individuals develop larger numbers of IgE antibodies when encountering these allergens and therefore are more likely to develop asthma and various other allergic reactions. Many of the allergens to which atopic individuals react which would not exert any pathological effect on non-atopic individuals. Atopy is at least partly genetic in nature, as can be seen from family and twin studies.[57]

7.2 Possible Role of Lanthanides in Asthmatic Reactions

There are many possible mechanisms by which lanthanides may induce asthma. A list of some pathologically feasible roles of lanthanides in asthmatic reactions follows.[58] These effects could induce asthma by acting alone or by acting in combination with other effects.

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[53] Leikauf.

[54] National Institutes of Health. National Heart, Lung, and Blood Institute. Lenfant, C, and Khaltaev, N. Global Initiative for Asthma: Global Strategy for Asthma Management and Prevention NHLBI/WHO Workshop (Based on a March 1993 Meeting). Publication Number 95-3659, January 1995.

[55] Galli, Stephen J. Immediate Hypersensitivity: Lecture in HST-175, Molecular and Cellular Immunology. Harvard-Massachusetts Institute of Technology Health Sciences and Technology Program. Boston, MA: November 5, 1996.

[56] Encyclopedia Britannica. Asthma. 1994.

[57] National Institutes of Health, 1995.

[58] Chan-Yeung, Moira. Occupational Asthma. Environmental Health Perspectives. 103 (Suppl 6), September 1995, 249 - 252.

1) Inhaled lanthanides may serve as allergens that specifically sensitize lungs and lead to specific IgE-dependent ashmatic reactions. These allergens may take the form of lanthanides alone or of metals complexed with other polllutants and/or human protein. This pathway would explain a significant effect of lanthanides on children, since allergic asthma often develops in childhood.
2) Lanthanide and/or lanthanide conjugates similar to those described above may lead to non-specific lung sensitization and/or hyperreactivity.
3) Lanthanides and/or their conjugates could bind constant regions of IgE antibodies on effector cells and induce cellular signaling as if specific antigen had bound the antibody. In support of this suggestion, Gd(III) has been shown to bind rabbit IgG constant regions.[59] This mechanism would allow lanthanides to preferentially increase the likelihood of atopic individuals to develop asthma, since these individuals would often have many effector cells sensitized with large relative amounts of IgE antibodies.
4) Lanthanides and/or their conjugates could stimulate cellular reactions occuring further along the asthmatic pathway, but still leading to inflammation, bronchoconstriction, and airway hyperreactivity.
5) Lanthanides could induce neural activities which lead to bronchoconstriction and other asthmatic symptoms.
6) Lanthanide emissions could increase asthma prevalence or severity in a very general, non-specific manner because they contribute to particulate pollution in the atmosphere and decrease air quality.
7) Lanthanides could specifically or non-specifically bind to other pollutants and assist the role of these pollutants in inducing asthma.

7.3 Related Studies

Many studies have investigated the toxicology of lanthanides as well as the role of particulates in respiratory disorders. Studies mentioned here comprise but a subset of such works and are provided to introduce the reader to related research.

Lanthanides have been shown to form reversible and ionic complexes with bioligands.[60] Such compounds could lead to antigen formation or to nonspecific stimulation.[61] Various animal

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[59] Dower, SK, Dwek, RA, McLaughlin, AC, Mole, LE, Press, EM and Sunderland, CA. The Binding of Lanthanides to Non-Immune Rabbit Immunoglobulin G and Its Fragments. Biochem. J. 149, 1975, 73 - 82.
[60] Evans, CH Biochemistry of the Lanthanides. 1990
[61] Leikauf, GD, Kline, S, Albert, RE, Baxter, S, Bernstein, DI, Bernstein, J and Buncher, CR. Evaluation of a Possible Association of Urban Air Toxics and Asthma. Environmental Health Perspectives. 103 (Suppl 6), September 1995, 253 - 271.

studies have shown lung changes which could be associated with chronic inflammation or asthma in animals upon exposure to lanthanides.

When extracellular calcium is present, histamine secretion induced by anit-IgE or by allergens is inhibited from 10^{-9} to 10^{-6}, induced at 10^{-4}, and inhibited at 10^{-3} M in rat cells.[62] Mast cell degranulation and acute inflammation were observed after injection of latnhanides into mouse skin.[63] This association of lanthanides with histamines and mast cells suggests that lanthanides could play a role in inducing or limiting asthmatic reactions, depending on the amount reaching the lung.

Associations between adult asthma and platinum salts, vanadium, cobalt salts, chromium salts, and nickel salts have all been observed in occupational settings.[64] IgE-dependent, non-IgE dependent, or non immunological mechanisms are all thought to play some roles in various kinds of occupational asthma. Multiple pathways exist by which these pollutants can cause bronchoconstriction. Among these are induction of inflammation due to general irritation and/or neural stimulation, and induction of IgE antibody production specific to the pollutant.[65] According to Kusaka, allergic asthma is induced by platinum, rhodium, nickel, cromium or cobalt via specific IgE antibodies and type I allergic reactions against human serum albumin complexed with one of these metals.[66]

Pritchard et al. studied the toxicity of first row transition metals in various particulate dusts including that from an oil-fired power plant, and found relationships between higher ionizable metal concentrations with oxidant formation and neutrophil influx, and reactivity and inflammation and susceptibility to infections in rats. Lung injury and hyperreactivity were caused by residual oil fly ash instillation in rats.[67] Like these transition metals, the lanthanides which have more than one stable valence state, such as cerium but not lanthanum, are also able to participate in electron transport and could catalyze similar bioreactions, leading to asthma. Or, it may be that conditions in the lung or atmosphere could allow lanthanum itself to participate in oxidation reactions. This study did not look for lanthanides in this fly ash, so it is not known whether a correlation would have been seen with lanthanide concentrations in fly ash.

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[62] Pearce, FL and White, JR. Effect of Lanthanide ions on Histamine Secretion from Rat Peritoneal Mast Cells. British Journal of Pharmacology. 72, 1981, 341 - 347.
[63] McClure 1980, in Evans, 1990.
[64] National Institutes of Health, 1995.
[65] Chan-Yeung, Moira. Occupational Asthma. Environmental Health Perspectives. 103 (Suppl 6), September 1995, 249 - 252.
[66] [Kusaka, Y. Occupational Diseases Caused by Exposure to Sensitizing Metals. Sangyo Igaku (KK9). 35: 2, March 1993, 75 - 87.] Abstract.
[67] Pritchard, RJ, Ghio, AJ, Lehmann, JR, Winsett, DW, Tepper, JS, Park, P, Gilmour, MI, Dreher, KL and Costa, DL. Oxidant Generation and Lung Injury after Particulate Air Pollutant Exposure Increase with the Concentrations of Associated Metals. Inhalation Toxicology. 8, 1996, 457 - 477.

Bronchoconstriction, and synthesis or release of acute inflammatory mediators can also caused be induced by animal exposure to air pollution particles.[68]

Many environmental studies have been conducted in order to assess the relationship between particulate matter in the air and respiratory diseases such as asthma. A study conducted by Gordian et al. in Anchorage, Alaska revealed a correlation between increased outpatient asthma visits and increased 10μm (PM10) particulates from non-anthropogenic sources, most likely largely crustal material from the earth. This suggests a relationship between coarse particulates and asthma. Many studies have shown a correlation between fine particulates and respiratory diseases, measured by asthma ER visits, childhood (<5) visits for asthma and bronchitis, and deaths due to COPD as well as daily mortality.[69,70] Dockery et al, however, did not observe an association between asthma and particulate concentrations in children in the Six Cities Study of Air Pollution and Health.[71]

The Childhood Respiratory Health Feasibility Study (CRHFS) conducted by the Minnesota Department of Health in 1988 observed a gradient of childhood asthma and other respiratory symptoms with distance from an industrial area exposing residents to refinery emissions. No correlation was found between the above gradient and measured refinery emissions such as SO2.[72] However, analytical methods used to detect emissions may not have been able to detect concentrations of lanthanides, though they were looking for heavy metal concentrations. It is possible that a gradient in levels of lanthanide exposure could explain the observed gradient in asthma prevalence, though no evidence of the above has been found.

Chapter 8: Conclusions and Suggestions for Future Research

8.1 Specific Conclusions from Multiple Analyses of Asthma Rates and Lanthanide Emissions

In evaluating whether lanthanides may have a causal effect on asthma in children alone or in the total population, conclusions from various sources of data must be brought together. Such conclusions from the various anaylses in our research are outlined below:

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[68] references in Ghio, AJ, Stonehuerner, J, Pritchard, RJ, Piantadosi, CA, Quigley, DR, Dreher, KL, and Costa, DL. Humic-like Substances in Air Pollution Particulates Correlate with Concentrations of Transition Metals and Oxidant Generation. Inhalation Toxicology. 8, 1996, 479 - 494.

[69] Gordian, ME, Ozkaynak, H, Xue, J, Morris, SS, and Spengler, JD. Particulate Air Pollution and Respiratory Disease in Anchorage, Alaska. Environmental Health Perspectives. 104: 3, March 1996. 290 - 297.

[70] Schwartz et al, 1996.

[71] Dockery, DW, Speizer, FE, Stram, DO, Ware, JH, Spengler, JD and Ferris, Jr, BG. Effects of Inhalable Particles on Respiratory Health of Children. American Review of Respiratory Disease. 139, 1989, 587 - 594.

[72] Minnesota Department of Health: Chronic Disease and Environmental Epidemiology Section. Childhood Respiratory Health Feasibility Study, Inver Grove Heights and Eagan, Minnesota. Final Report to the Minnesota Legislature. June 27, 1991.

1) *Comparisions between National Asthma Hospitalization Rates and Measures of Lanthanide Emissions:* A general increase in national trends for childhood and total asthma hospitalization rates has been observed. Increases in lanthanide usage have also been seen, which led to the initial proposal of the hypothesis being tested. Though a general correlation between asthma rates and lanthanide trends is sometimes observed, specific decreases in lanthanide emissions are not reflected in asthma rates.

Conclusions: Lanthanides may have been involved in the increase in asthma rates in the 1970s, but do not appear to directly dictate specific trends in asthma.

2) *Regional Comparisons between Asthma Hospitalization Rates and Lanthanide Emissions:* Counties with unexplainably high asthma hospitalization rates can be pinpointed. The increase in national childhood and total asthma rates is also seen on a regional level, and is especially pronounced for the Northeast. Regional analyses of lanthanide emissions show some increases, but drop or remain constant during the time periods of increase in the Northeast. However, the relative amounts of emissions are often higher in the Northeast than in the other regions, which correlates with asthma rate distributions. Furthermore, the region with the highest percentage of oil states is also the Northeast. Special notice must be taken of the fact that the specific division of the nation into the four regions used by the NCHS might blur correlations between regional asthma rates and regional lanthanide emissions, due to a lack of separation between oil versus coal and gas states in these regional divisions.

Conclusions: As can be seen to some extent in the Northeast, an overall regional correlation may exist between the magnitude of average asthma rates and the magnitude of lanthanide emissions. Such a clear relationship might not have been observed for regions in our analyses due to the actual regional divisions established by the NCHS.

3) *Lanthanide Deposition in Human Hair:* Studies of human hair in one community do not reflect increased levels of exposure to lanthanides in that community.

Conclusions: The actual exposure to lanthanides does not appear to have increased in a community where an increase in lanthanide emissions is expected to have occurred, suggesting that lanthanides do not have an effect on human health.

4) *Lanthanide Deposition in Bodies of Water:* Increases in lanthanide depositions in sediment are not seen, though such increases may be observable in wetlands.

Conclusions: Further work needs to be done in wetlands in order to determine whether expected increases in lanthanide emissions are actually increasing the amount of lanthanides escaping to the atmosphere.

5) Related Works: Related works support the hypothesis that the addition of lanthanides probably plays a role in respiratory disorder through nonspecific particle pollution. However it is not clear whether these metals play a specific role in the induction of asthma.

Conclusions: Many additional related studies of lanthanide toxicity and bioreactivity exist and may provide further clues to potential roles of lanthanides in asthma prevalence. Studies of mechanisms by which other metals specifically induce asthma suggest that lanthanides could do the same.

8.2 Overall Conclusion: Does a Causal Relationship Exist?

Measures of lanthanide deposition in human hair and in sediment, as well as specific changes in estimates of lanthanide emissions and in asthma hospitalization rates, suggest that a specific causal relationship between lanthanide exposure and asthma prevalence does not exist. However, increases in lanthanide depositions can be seen in a wetland in the Northeast, and an undeniable correlation seems to exist between the high levels of asthma rates and lanthanide emissions in the Northeast. Though this latter correlation could be an incidental finding due to the large amount of pollutants emitted in the Northeast, it is possible that lanthanides are one of many factors influencing asthma prevalence rates in the this region. The role of lanthanides in the Northeast may even be more pronounced in this region due to an association with other environmental agents found in the Northeast. Lanthanides might also play similar roles in other regions of the nation, though this may not have been observable due to the pre-established regional divisions by which comparisons were constrained.

The pathology of asthma is very complicated and mechanisms causing the disorder are not fully understood. Many environmental agents can be involved in causing asthma, especially in children, who tend to spend greater proportions of their times outdoors and are thus influenced by both outdoor and indoor air pollutants. Lanthanides may play specific roles in inducing asthma, though evidence for this is unclear. It is probable that lanthanide emissions have at least a small effect on asthma prevalence rates not necessarily because of specific properties associated with these metals, but due to a the general decrease in air quality caused by their emissions. This effect may be negligible, however, and may be masked by larger effects of other pollutants or environmental factors.

8.3 Suggestions for Further Research

Further research must be conducted in order to establish for certain whether lanthanide emissions have an effect on asthma prevalence. Such research needs to focus on four main areas:

1) Human Exposure: Hair and possibly lung tissue samples should be collected from other communities in order to definitely establish whether exposure to lanthanides is increasing in humans. This is the most important factor to be determined, since if human exposure does not increase even under the effect of increased emissions, there can be no causal relationship. J. Abraham of the Department of Pathology at the SUNY Health Science Center in Syracuse, New York has a large database of information from over 600 lungs which he has already studied for occupational and pathological associatinos with Fe, Ti, Al and Cr.[73] Perhaps a search through his database for lanthanide concentrations in lung samples would provide clues to the effects of these metals.

2) Wetland Deposition: Though lanthanide emissions can be esitmated, the actual amounts of lanthanides reaching a community needs to be determined. Wetland cores should be analyzed in order to evaluate whether the suggested increase observed in our limited wetland data can be seen in more detailed and statistically accurate analyses. States with more detailed asthma records should be chosen for analysis. Perhaps Minnesota would be a particularly good state in which to do such analyses, since concentrations could be compared along the observed gradient of asthma prevalence, provided that wetlands exist in those ares. Furthermore, an understanding of why increases in lanthanide concentrations were not seen in our sediment cores should be developed.

3) Lanthanide Emissions: Estimates of lanthanide emissions should be normalized to population or area in order to provide better comparisons with asthma rates in different states and regions. Further measures of lanthanide usage should also be obtained, so that regional and even state wide estimates of lanthanide emissions can be made. For example, estimates of emissions from motor vehicles for rural versus urban regions within states would be useful to investigate the effect of motor vehicle emissions alone. The time period in which different converters were used would also be helpful, as would a knowledge of when Japanese cars, which unlike American cars use more lanthanum than cerium, implemented the use of lanthanides in catalytic converters.

4) Asthma Epidemiology: State and county hospital discharge rates over the last few years are available for many states, and should be used to compare statewide asthma rates with statewide

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[73] Abraham, JL, Hunt, A, and Burnett, BR. Lung Pathology and Mineralogy Associated with High Pulmonary Burden of Metal Particles: Fe, Ti, Al, and Cr in a Pneumoconiosis Database. Inhaled Particles VIII, 1997, in press.

estimates of lanthanide emissions. Such data may need to be adjusted for the age demographics in the state or county of interest, and care must be taken to obtain rates adjusted using the same methods.[74] Such analyses could allow us to better understand the regional comparisons previously discussed. If counties of interest are located, research into hospitalization patterns in those communities could be conducted in order to determine trends in asthma prevalence dating further back than the available hospital discharge statistics. Also, the NHIS generates State Data Files (CDRom Series 10 # 4a) which should be checked to see if they contain asthma statistics. Furthermore, mortality rates due to asthma by state and region could also be analyzed, and mortality: prevalence ratios could also be generated in order to estimate trends in severity. Such analyses would require the use of mortality and prevalence rates for same age groups.

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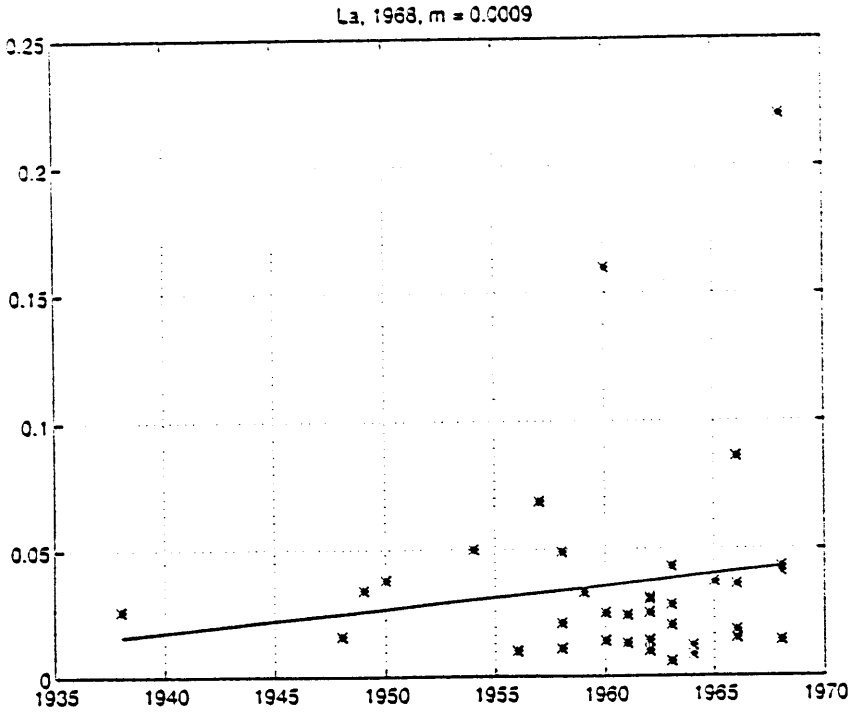
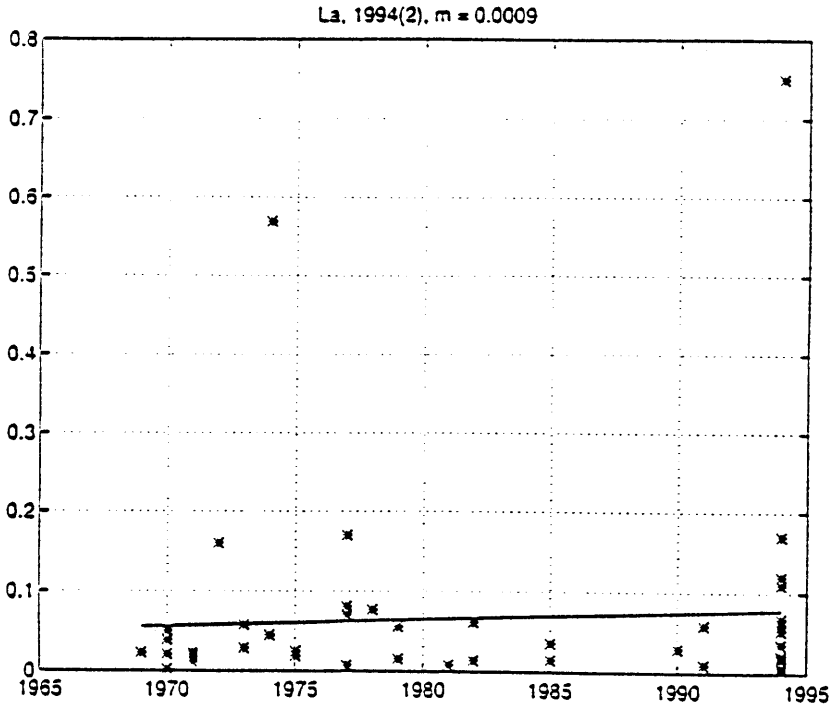
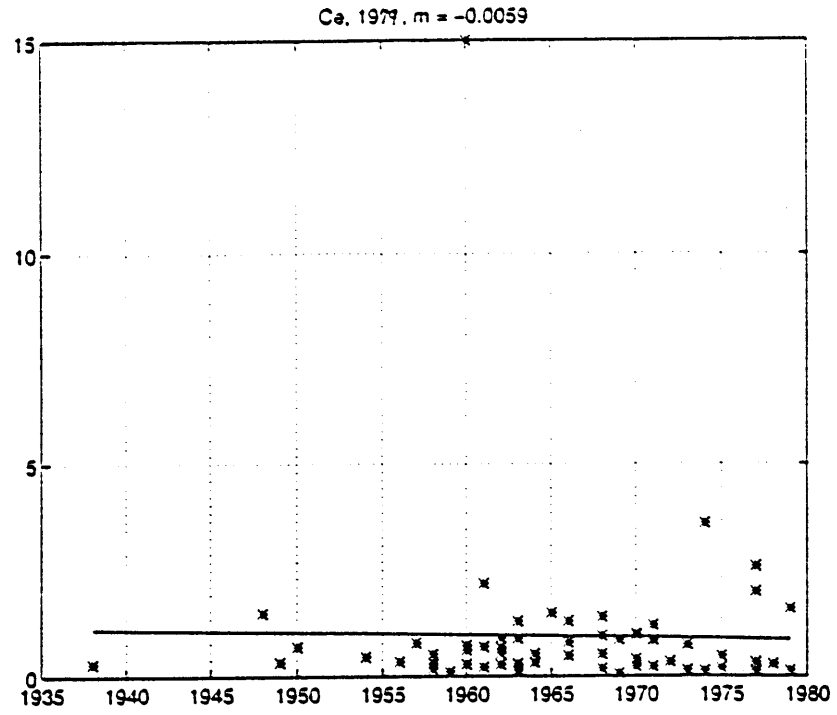
Appendix A: Useful Contacts

- Dr. Mark Utell (716) 275 - 4861 University of Rochester
- Jim L'Omeara (518) 474-3189 New York State Department of Health Bureau of Biometrics. Hospital discharge statistics
- Bill Allen (6170 451-5340 x397 Massachusetts Department of Health. Hospital discharge statistics.
- Bob Scardamalia (518) 474-1141 Empire State Development. New York population estimates.
- Richard Senicola (617) 890-6040 Massachusetts Health Data Consortium. Hospital discharge statistics.
- Juliet vanEenwyk Washington Department of Health. Noninfectious Disease Epidemiology, Hospital discharge statistics. (360) 705-6051
- Dr. Kevin Weiss (312) 942-3576 Rush Institute for Primary Care. Center for Health Services Research.
- National Center for Health Statistics (301) 436 - 8500
- John Horm (301) 436-7085 x123 National Center for Health Statistics Survey Planning and Development
- American Lung Association 1-800-LUNG-USA

Appendix B: Sample Plots and Regression Analyses of Hair Data



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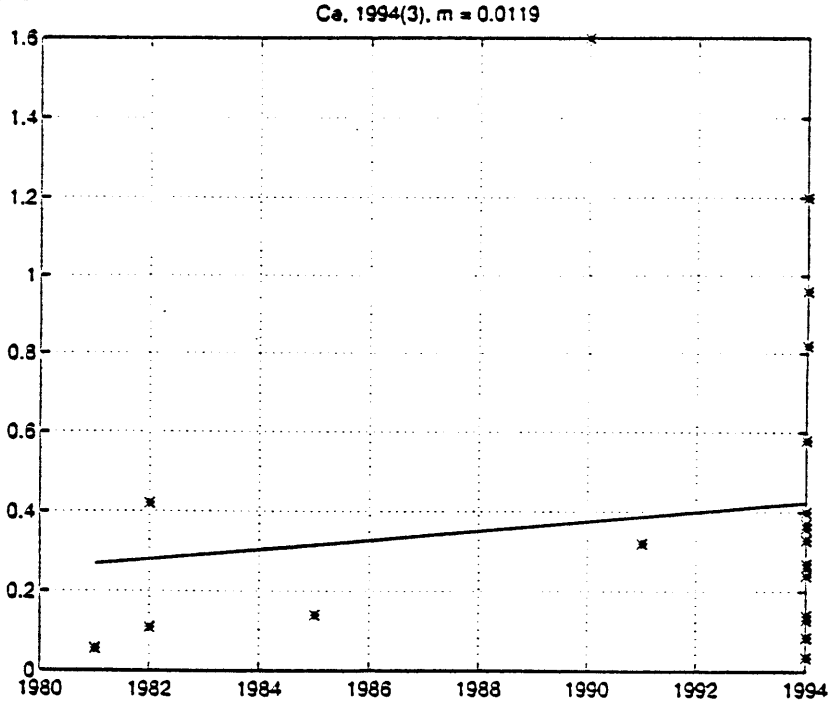
15
10
5
0
1935
1940
1945
1950
1955
1960
1965
1970
1975
1980


Ca, 1994(3), m = 0.0119
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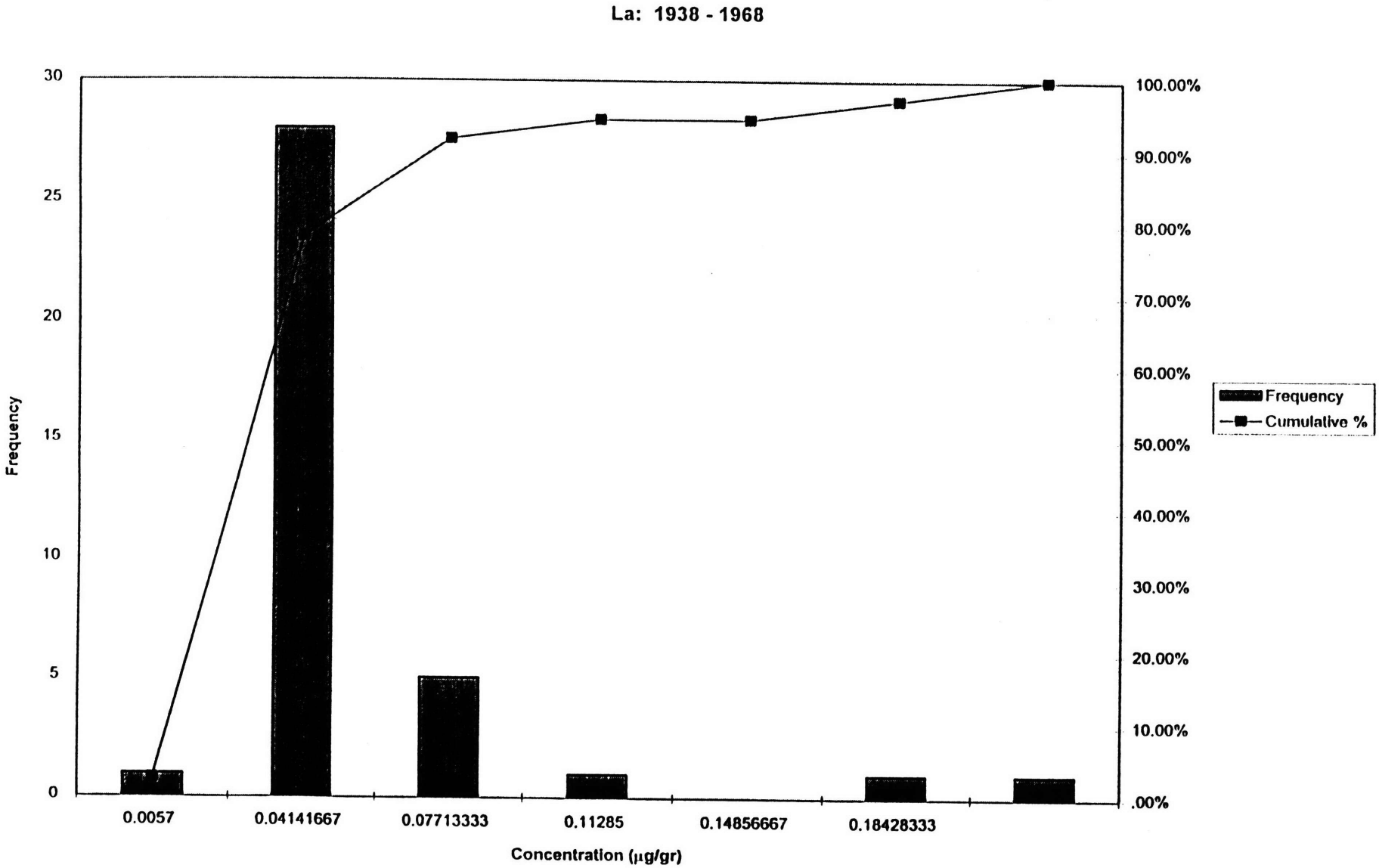
1.2
1
0.8
0.6
0.4
0.2
0
1980
1982
1984
1986
1988
1990
1992
1994


La: 1938 - 1968
30
25
20
15
10
5
0
Frequency
100.00%
90.00%
80.00%
70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
.00%
Frequency
Cumulative %
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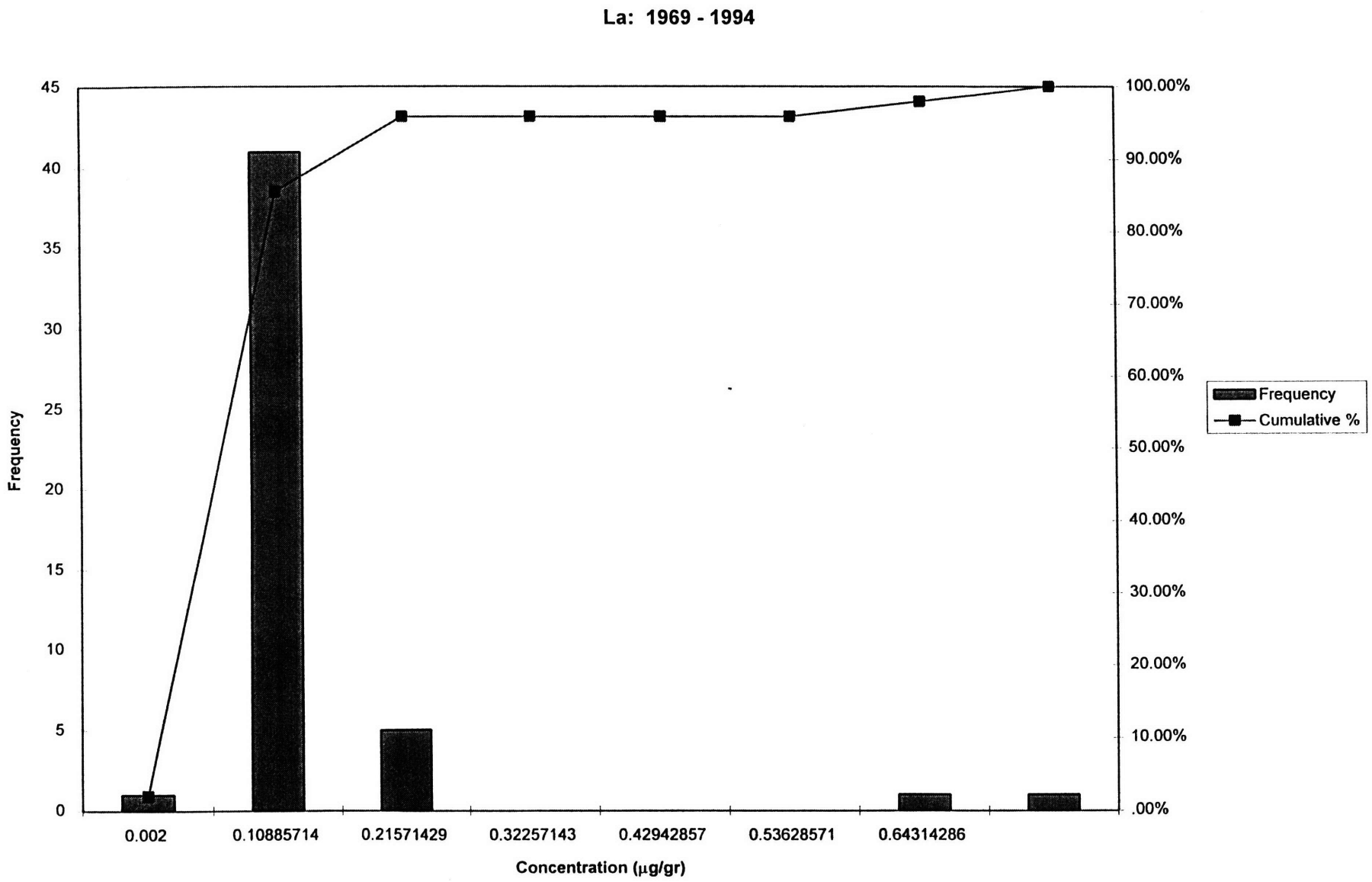
0.14856667
0.18428333
Concentration (µg/gr)


La: 1969 - 1994
Frequency
45
40
35
30
25
20
15
10
5
0
100.00%
90.00%
80.00%
70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
.00%
Frequency
Cumulative %
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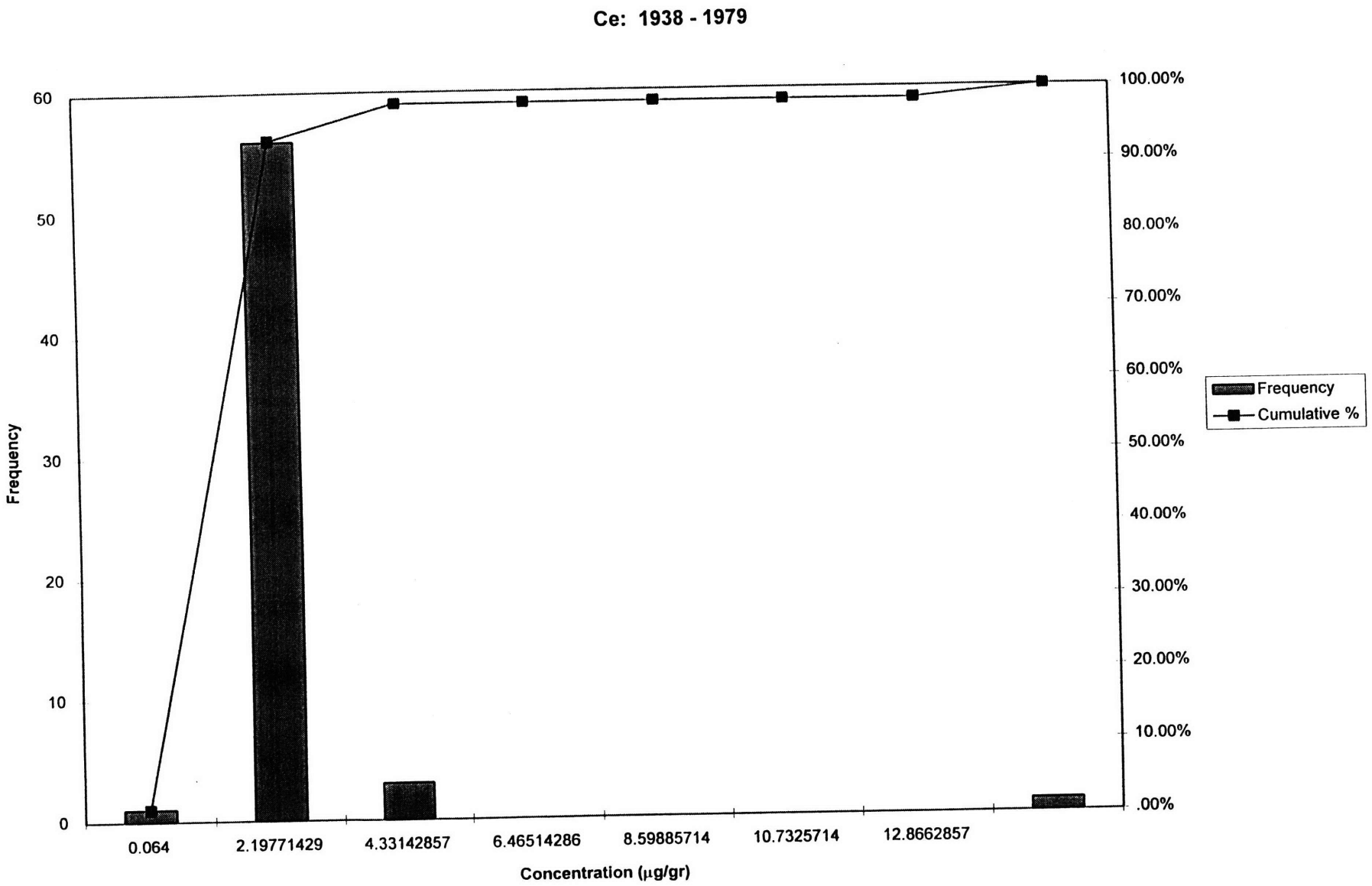
0.42942857
0.53628571
0.64314286
Concentration (µg/gr)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60
50
40
30
20
10
0
Frequency
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90.00%
80.00%
70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
.00%
Frequency
Cumulative %
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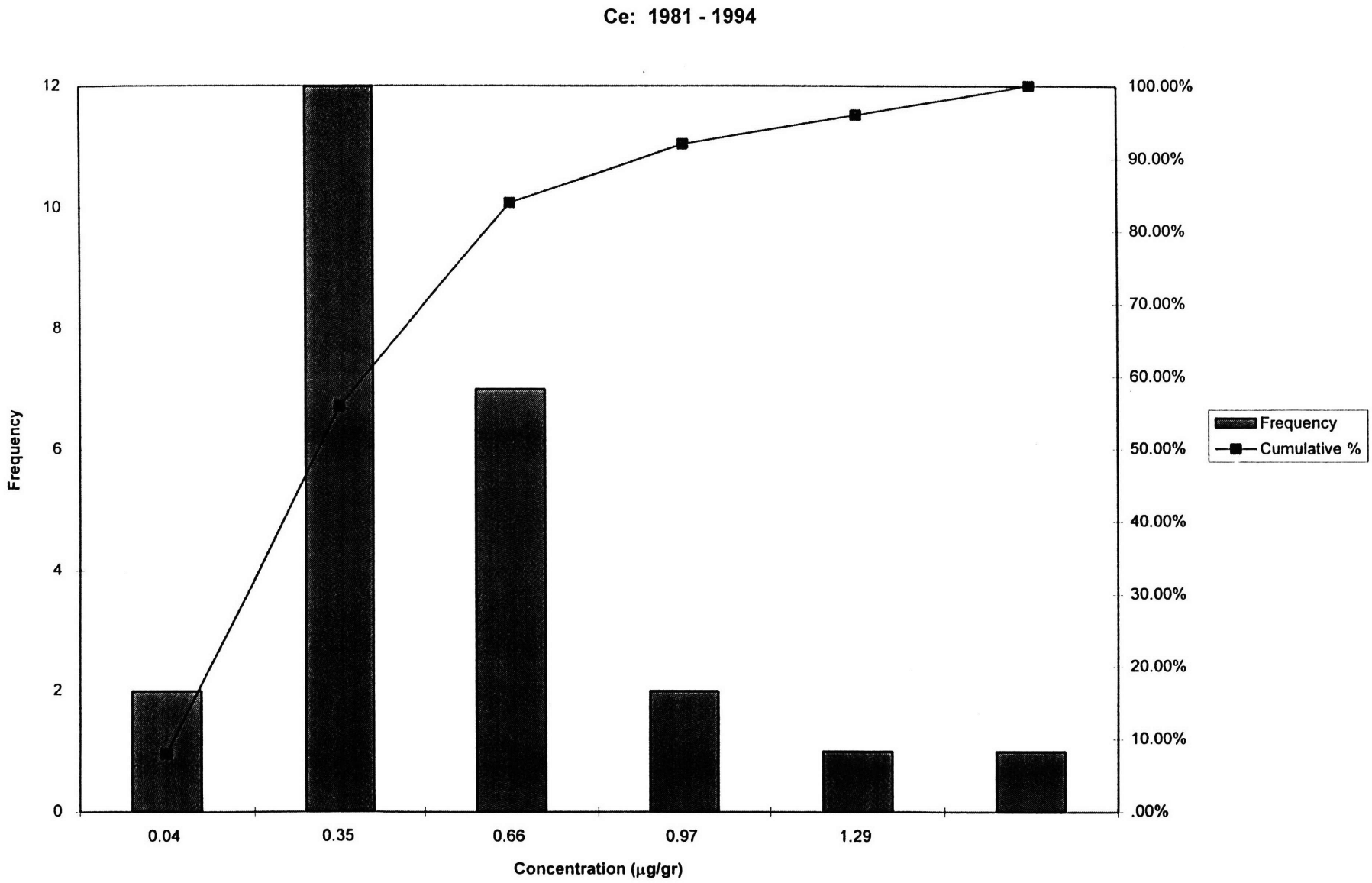
12.8662857
Concentration (µg/gr)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10
8
6
4
2
0
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70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
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Frequency
Cumulative %
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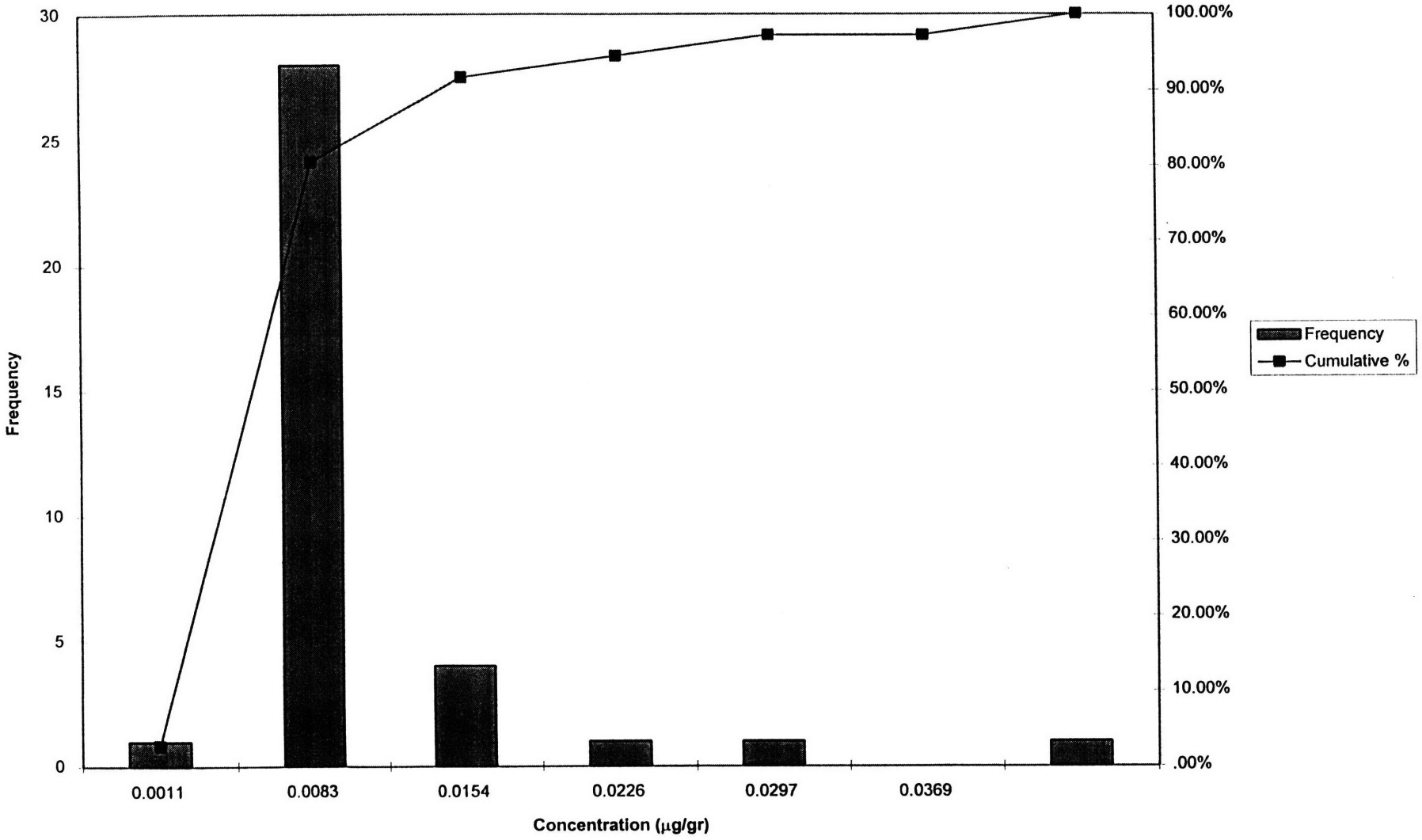
0.35
0.66
0.97
1.29
Concentration (µg/gr)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Frequency
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50.00%
40.00%
30.00%
20.00%
10.00%
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Frequency
Cumulative %
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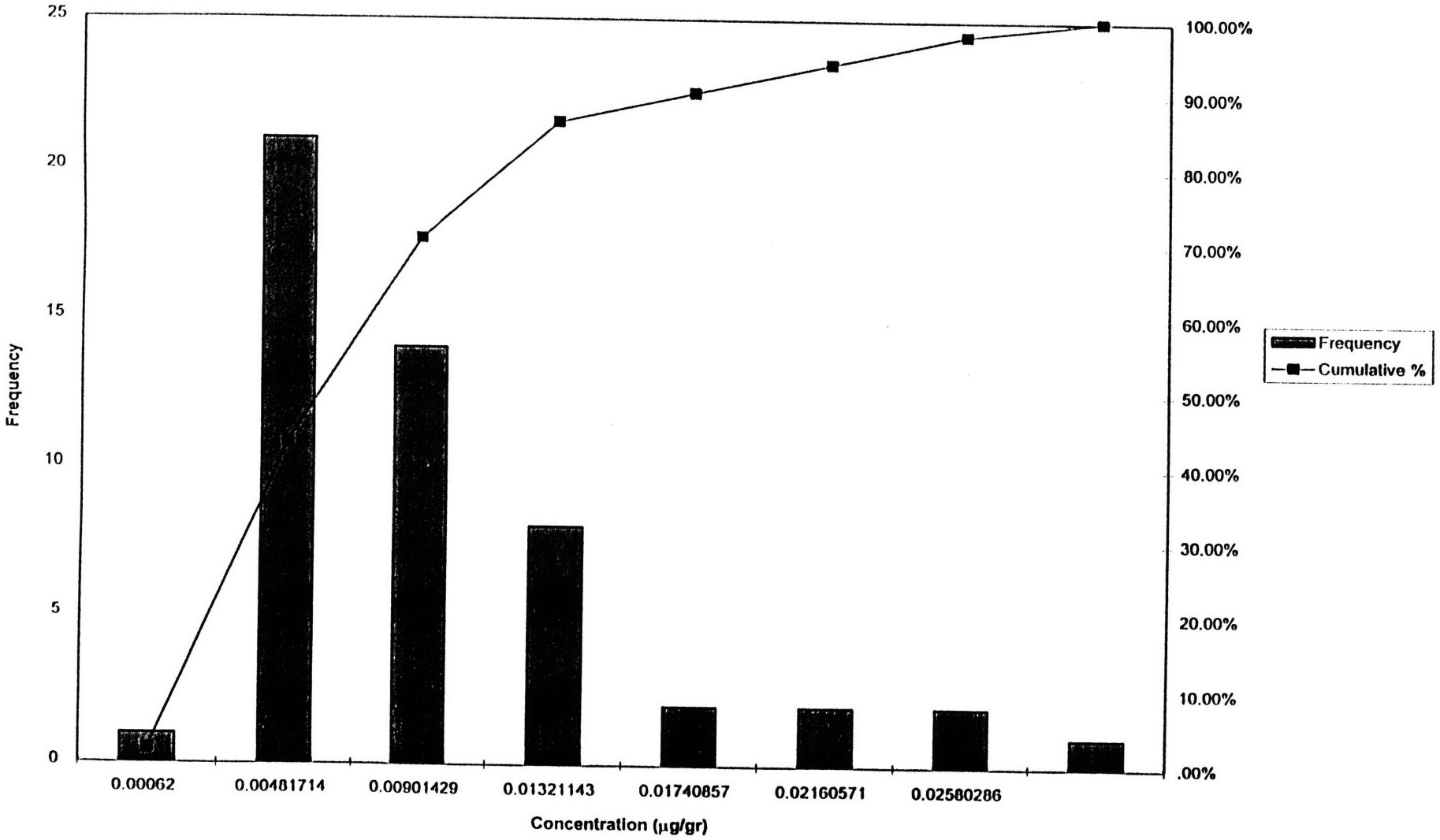
0.0226
0.0297
0.0369
Concentration (µg/gr)


Sc: 1969 - 1994
25
20
15
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Frequency
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80.00%
70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
.00%
Frequency
Cumulative %
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0.01740857
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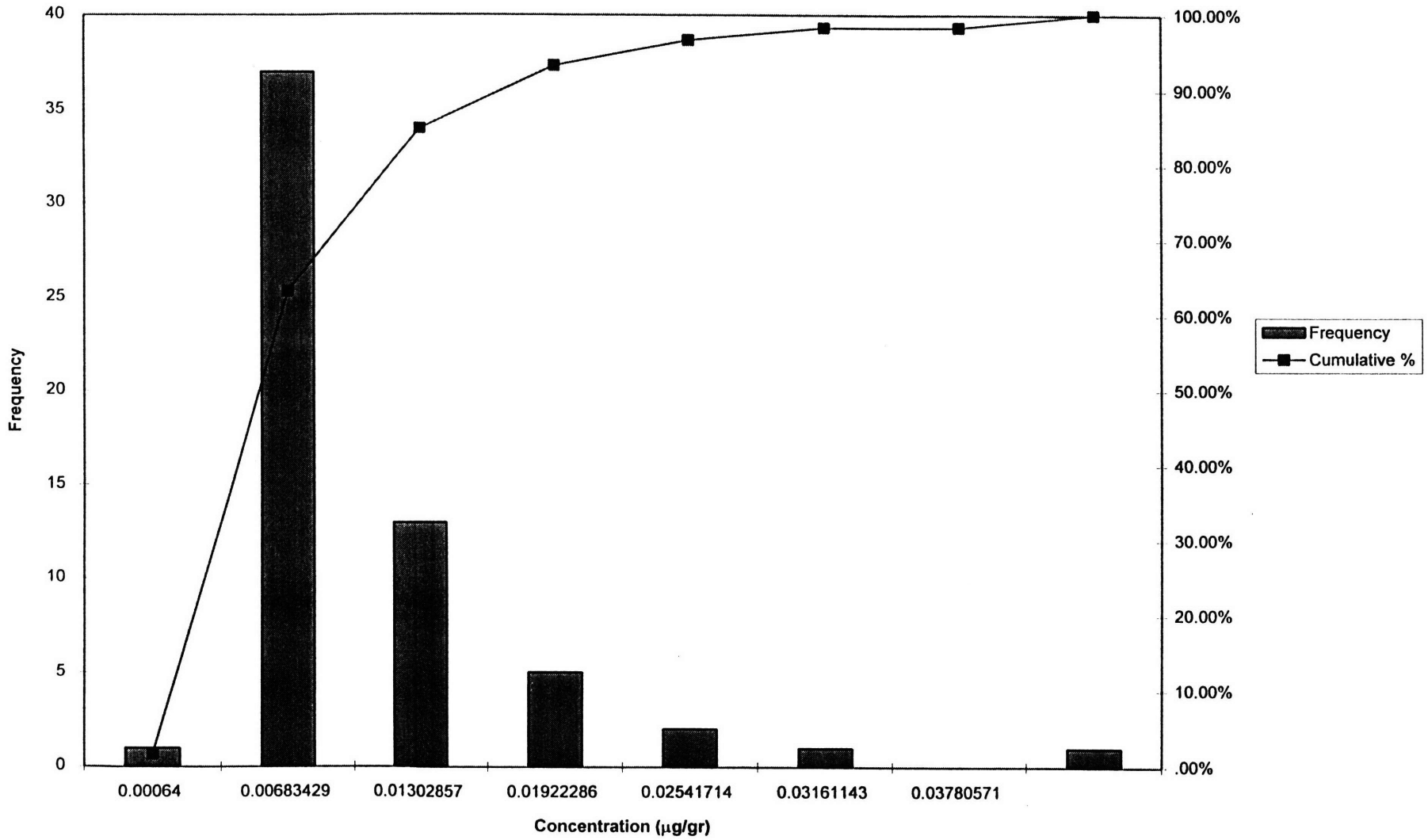
Concentration (µg/gr)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5
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Frequency
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60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
.00%
Frequency
Cumulative %
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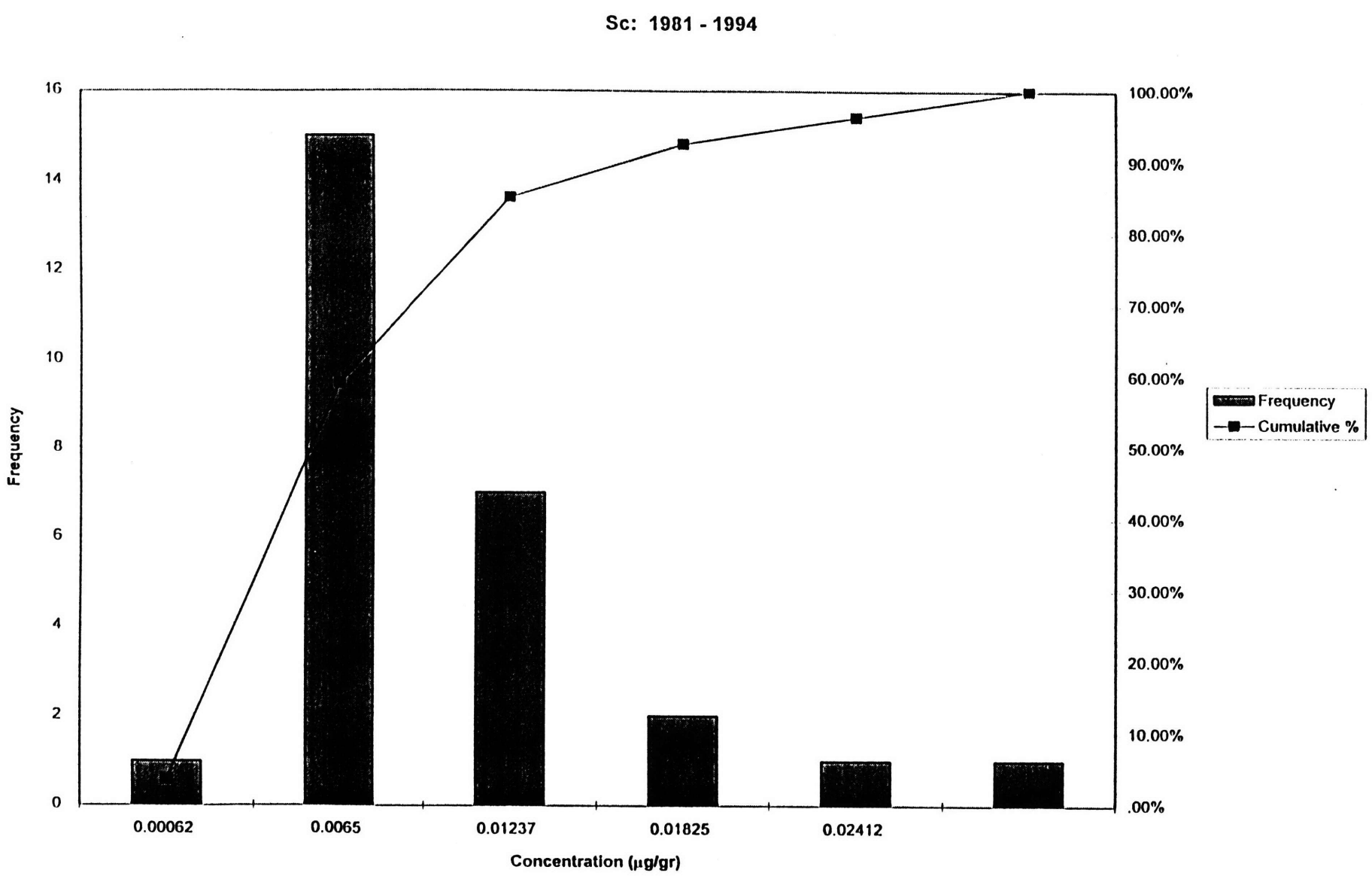
Concentration (µg/gr)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16
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60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
.00%
Frequency
Cumulative %
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0.0065
0.01237
0.01825
0.02412
Concentration (µg/gr)