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RESEARCH PAPERS ON GEOGRAPHIC ASPECTS OF DISEASE
PART A: GEOGRAPHIC ASPECTS OF THE CONTROL OF MEASLES:
WITH SPECIAL REFERENCE TO MICHIGAN
PART B: GEOGRAPHIC ASPECTS OF HYPERTENSION

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Two diseases, measles and hypertension, are examined from a geographic perspective. Although officially a "preventable" disease, measles has yet to be brought fully under control in the United States, particularly in Michigan. Geographic approaches to the control of measles, such as planar graph analysis, diffusion modelling and multiple-scale target area approaches are recommended. Epidemiologic and etiologic aspects of hypertension are also discussed. Multiple-scale spatial analysis and interdisciplinary approaches to disease modelling are suggested as ways to improve the identification of high-risk populations and high-risk environmentable variables.

ABSTRACT

GEOGRAPHIC ASPECTS OF THE CONTROL OF MEASLES:
WITH SPECIAL REFERENCE TO MICHIGAN

By

Debbie L. Borchers

The history and current status of measles and its control strategies in the United States and in Michigan in particular reveal that, although officially a "preventable" disease, it has not yet been brought fully under control, despite the availability of an effective vaccine. Epidemiologic studies reveal that attack rates of measles are highest among blacks, persons of lower socio-economic status, inner city residents, and the most densely populated areas. Regionally, the highest rates are found in the East North Central states. Michigan, which had the largest absolute number of cases in 1978, and the second highest rate in the country, is examined in this paper. Spatial analysis shows that Michigan's susceptibility rates steadily increased from 1976 to 1979, and that clustered high-risk populations created a situation favorable for the rapid diffusion of measles. Different geographic approaches to disease control and compliance problems, such as planar graph analysis, diffusion modelling and multiple-scale target area approaches, are recommended.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

Figure | Page

I. INTRODUCTION

Although measles is an infectious disease easily preventable by vaccination, epidemic outbreaks continue to occur throughout the United States. Reported cases of measles dropped 95 percent between 1963, when the first measles vaccine was licensed, and 1968, leading many public health authorities to believe that eradication of the disease was possible (Riley, 1976). Increasing rates of measles and other vaccine-preventable diseases since the early 1970s, however, have diminished hopes of eradication.

Studies of epidemic outbreaks have revealed a non-random spatial pattern of measles in the United States. Higher incidence of measles occurs in black populations (Landrigan and Conrad, 1971; Currier et al., 1972; Pyle, 1973) and in areas of lower socioeconomic status (Landrigan and Conrad, 1971; Schiff et al., 1975; Pyle, 1973). In addition, attack rates vary between urban, rural and suburban areas (Landrigan and Conrad, 1971; Cherry et al., 1972). Regional concentrations of measles cases on a national scale are also evident. In the late 1970s, the East North Central states reported the largest numbers of cases and the largest percentage increases in measles incidence (Halpin et al., 1977).

Since the development of an effective medical control measure, that is, the vaccine, has failed to bring measles under control, other

approaches are needed to stop further unnecessary outbreaks. Evidence of spatial variations in measles incidence suggests that the degree to which the disease is controlled varies according to different segments of the population and different geographic areas. This paper therefore presents a geographic approach to the problem of the control of measles, with special emphasis on the control problem in Michigan. Michigan was selected as an area of interest because of its particularly poor record of measles control; approximately one-third of the nation's entire measles cases in 1978 occurred in Michigan (Center for Disease Control, 1979).

The literature review of historical and epidemiological studies and the data presented in this paper are the result of an attempt to investigate the spatial distribution of measles in the United States and to examine the effectiveness of various disease control strategies. Section II provides the historical background of the development of immunization procedures and public health campaigns that paved the way for the possible eradication of many infectious diseases, including measles. The development of specific public health campaigns in Michigan is included in order to place the current control problem in perspective for that state. Section III consists of a description of the clinical significance of measles, a discussion of the diffusion process of epidemics and a literature review of current epidemiologic studies of measles in the United States. The epidemiology of measles in Michigan is also examined in the third section, with an emphasis on the 1978 epidemic and the levels of immunity and susceptibility in the population from

1976 to 1979. Various approaches to the prevention and control of measles in the United States and Michigan are examined in Section IV, including a cost-benefit analysis of immunization programs in general. Section V includes a discussion of selected geographic approaches to the improvement of disease control and compliance behavior. Spatial analytical techniques and diffusion models are suggested as methods that can be used to bring a disease such as measles under control and prevent future outbreaks. Finally, Section VI presents a summary of the previous sections and a discussion of final conclusions.

II. THE HISTORICAL DEVELOPMENT OF IMMUNIZATION AND ITS EFFECT ON INFECTIOUS CHILDHOOD DISEASES

The Development of Immunization Procedures in the United States

Most people today have never seen a case of smallpox or remember a child dying from measles. Yet the infectious diseases of childhood which are now preventable with vaccines contributed greatly to morbidity and mortality rates in the past. The development of specific vaccines has lessened the dangers associated with many of these diseases and has apparently eliminated one altogether, namely, smallpox. It is perhaps partly due to this lack of visibility of certain diseases in society that has led people to become complacent about fulfilling immunization requirements. The history of childhood diseases shows, however, that they were at one time both prevalent and lethal.

Smallpox, measles, diphtheria and whooping cough (pertussis) had particularly high mortality rates in the United States in the nineteenth century (Table 1). The number of deaths from these diseases remained high through the end of the nineteenth century and on into the mid-1900s, except for smallpox which showed quite a dramatic decrease in deaths between 1870 and 1880 (Table 2). Death rates were not available for these years, but the large difference in the number of deaths from smallpox between 1870 and 1880

TABLE 1.--Mortality Rates for Specified Diseases in the United States, 1850-1870.

Disease	1850		1860		1879	
	No. of Deaths	Death Rate*	No. of Deaths	Death Rate*	No. of Deaths	Death Rate*
Smallpox	2,352	10.1	1,271	4.0	4,507	11.7
Measles	2,983	12.9	3,899	12.4	9,237	23.9
Diphtheria	N.A.	N.A.	1,663	5.3	6,303	16.3
Whooping Cough	5,280	22.8	8,408	26.7	9,008	23.4

SOURCE: Ninth Census of the United States, Reports - Vital Statistics, 1870.

*Number of deaths per 100,000 population.

TABLE 2.--Deaths from Specified Diseases in the United States, 1880-1900.

Disease	1880[a]	1890[b]	1900[c]
Smallpox	871	N.A.	3,484
Measles	8,072	9,256	12,866
Diphtheria	38,143	41,677	16,475
Whooping Cough	11,064	8,432	9,958

SOURCES: [a]Tenth Census of the United States, Mortality and Vital Statistics, Part I, 1880.

[b]Eleventh Census of the United States, Mortality Statistics, Part II, 1890.

[c]Twelfth Census of the United States, Vital Statistics, Part II, 1900.

is probably due to the introduction and acceptance of the smallpox vaccine. Some of the decrease may also be attributed to changes in the methods of disease reporting during the 1870-1880 decade. Measles, currently considered a rather mild childhood disease by most people, claimed nearly 13,000 lives at the turn of the century.

The distribution of these diseases among the population remained essentially the same until the process of immunization was developed. This process involves "conferring increased resistance (or decreased susceptibility) to infections" and can be either passive or active (Parish and Cannon, 1962, p. 5). Passive immunization consists of preparing immune sera (which contain ready-made antibodies) to help cure infectious disease. Reactions within an infected person take place rapidly, even though protection is often temporary. Active immunization, on the other hand, involves the administration of toxins, toxoids and vaccines which help to produce antibodies and prevent a specific disease from occurring. This particular process takes more time to develop than passive immunization and is also capable of conferring protection for longer periods of time (Parish and Cannon, 1962).

The idea of conferring protection against infectious diseases actually goes back hundreds of years. The Chinese placed dried crusts from the skin of smallpox patients into the nostrils of healthy persons so that they would develop a weakened form of the disease, thereby conferring lifelong immunity (Reidman, 1974). This Chinese practice had gone on for centuries but was made popular in the western world by Lady Mary Wortley Montague of England.

While living in Turkey in the early 1700s, she noticed the women grafting smallpox matter from the end of a needle onto the patient's skin. This particular method, like the Chinese method, is known as variolation or inoculation and produces a milder form of the disease than would occur if one were infected naturally. This method gradually led to a decline in the mortality rate from smallpox (Reidman, 1974).

The first form of vaccination was introduced into the United States in 1796 by Edward Jenner. The word vaccination was used at this time to distinguish Jenner's method from the previously used term, inoculation, associated with smallpox matter. Jenner injected a young man with pustule matter from a cowpox patient, then later inoculated the same individual with some smallpox fluid. After a series of experiments, Jenner was able to prove that people with cowpox were immune to smallpox and by administering a certain amount of cowpox matter, people could be protected from smallpox (Reidman, 1974).

Nearly a century passed before another vaccine was developed. Loeffler discovered the diphtheria bacillus in the 1880s and shortly thereafter Roux and Yersin discovered the diphtheria toxin (Reidman, 1974). The first diphtheria antitoxin was administered in Berlin in 1891. Another important breakthrough for diphtheria occurred with the development of the Schick test (Reidman, 1974). Bela Schick found that people who had recovered from diphtheria retained antibodies in their serum for life. A test was therefore developed that could detect the susceptible population and thus prevent

diphtheria by shots of toxin. Other major events in the development of vaccines and immunization are listed in Table 3.

As the knowledge of bacteria, viruses and vaccines proliferated, the morbidity and mortality rates of common childhood diseases declined. Advances in medical technology alone, however, proved insufficient to combat these diseases. Fear and ignorance hindered many people from accepting vaccination as a way to prevent disease. A group of "anti-vaccinationists" was formed in the early part of the nineteenth century, fearing that vaccines were unpure and would be more harmful than the disease itself (Reidman, 1974). Thus, although Jenner's first successful vaccination occurred in 1796, many states had problems enforcing vaccination requirements well into the nineteenth century. An examination of immunization campaigns in one state, Michigan reveals some of the challenges that have confronted public health workers during the vaccine era.

The Development of Immunization Campaigns in Michigan

Michigan established a set of rules in 1875 recommending smallpox vaccination for every child under two years of age and for all other persons once every five years. Vaccinations were required for all new employees of incorporated manufacturing companies and for all children entering school. Nevertheless, compliance with these rules was often ignored and led one doctor to complain that

> . . . the very great extent by which the sickness and death rate is reduced in this country through vaccination can hardly be appreciated by our people who have never seen the fearful ravages of smallpox. . . . Some persons do not seem

TABLE 3.--Important Dates in Immunization Development.

Year	Development
1721	Lady Montague introduced variolation into England from Turkey.
1709	Jenner published work on vaccination.
1880	Existence of diphtheria toxin proved at Pasteur Institute by Roux and Yersin.
1890	Behring and Kitasato discovered diphtheria antitoxin.
1890	Behring and Kitasato proved animals could be immunized by repeated doses of tetanus toxin.
1904	Tetanus antitoxin began to be used prophylactically to treat wounds in the United States.
1906	Calmette and Guerin of the Pasteur Institute advocated BCG for tuberculosis.
1908	Mantoux described diagnostic test for tuberculosis in France.
1913	Schick introduced diagnostic test for diphtheria.
1925	Serum prophylaxis for measles introduced into Great Britain by Copeman.
1927	Tetanus toxoid used for human immunization (Paris).
1940	Pertussis vaccine distributed in Michigan.
1942	National immunization campaign for diphtheria.
1944	Human immune serum globulin for measles introduced into the United States by Cohn.
1947	Gamma globulin being used with success in the United States.
1948	Compulsory smallpox vaccination of infants ended in Great Britain.
1953	Salk prepared polio vaccine.
1954	National Foundation for Infantile Paralysis, Inc. introduced nationwide trial of Salk vaccine.
1956	Pertussis vaccine became first bacterial vaccine to be internationally standardized.
1962	World Health Organization initiated worldwide smallpox eradication scheme.
1963	Measles vaccine licensed in the United States.
1967	National eradication campaign for measles started.

SOURCE: Adapted from H. J. Parish and D. A. Cannon, Antisera, Toxoids, Vaccines and Tuberculins in Prophylaxis and Treatment, E. & S. Livingstone Ltd., Edinburgh, 1962, pp. 274-302.

> capable of grasping the problem, and of appreciating the overwhelming evidence of the utility and comparative safety of the operation (Michigan State Board of Health, 1875, p. xxiv).

Prior to the existence of a state vaccination law in Michigan, various vaccination campaigns were carried out. As early as 1837 a severe smallpox epidemic in Detroit prompted a local physician to begin a general vaccination campaign in the city. He further extended his services to the neighboring Indian tribes; 600 Saginaw Indians were vaccinated in 2 days (Michigan State Board of Health, 1875). Another campaign in Detroit during the summer of 1877 resulted in the vaccination of 16,000 persons by the Public Health Department at a cost of $4,015. Private physicians reportedly had vaccinated just as many people during the same period (Michigan State Board of Health, 1877).

After much debate concerning a compulsory immunization law, the Michigan State Board of Health passed a law in 1879 stating that physicians must offer vaccinations every year, without cost to persons vaccinated, at the general expense of the locality (Michigan State Board of Health, 1879). Some people felt that a stronger law requiring people to be vaccinated would impinge on personal rights of self-determination and control. Others felt the 1879 law was too weak and further measures were warranted. One suggestion was to establish a "vaccine farm"--a vaccine-producing operation to be maintained by Michigan Agricultural College (now Michigan State University) and to provide for the delivery of public vaccination to every house once a year

(Michigan State Board of Health, 1877). In 1894, the Secretary of the State Board of Health stated that sending physicians out to families to offer free vaccinations was "the best way to induce people to be vaccinated" (Michigan State Board of Health, 1894, p. 356). One physician suggested making parents who refused vaccination for their children subject to a fine of not less than five dollars or ten days in jail for each offense (Michigan State Board of Health, 1894). Beginning in 1875 all children were required to be vaccinated before entering school, but reports of enforcement were rare. One report states that a rigidly enforced exclusion-from-school program in Detroit resulted in the absence of smallpox among the 12,000 school children in the city of 1882 (Michigan State Board of Health, 1882).

For the most part, campaigns at this time consisted of the distribution of pamphlets and leaflets on the prevention of smallpox. These were usually sent out to areas where outbreaks occurred or where they were expected to occur, including lumbering camps throughout the state which had new crews of workers every fall (Michigan State Board of Health, 1885). Organized immunization efforts at the state level were not effective until the Bureau of Epidemiology was created after the turn of the century. Free vaccination clinics were held in a number of places throughout the state. During the summer of 1924 a total of 47,536 persons were vaccinated by State Health Department members (Michigan State Board of Health, 1925-26). Local private physicians also reportedly vaccinated thousands of individuals at this time. Thus, 70 percent

of the population of Lansing and its vicinity (91,845 persons) were vaccinated from June 1 to June 20, 1924 (Michigan State Board of Health, 1925-26).

The Michigan Department of Public Health began a statewide campaign for protection against diphtheria in January of 1925 (Michigan State Board of Health, 1925-26). Toxin-antitoxin was administered free of charge at scheduled immunization clinics throughout the state. In 4 counties alone, 11,506 children and adults were immunized. Additional diphtheria projects were carried out in 7 counties and 25 cities and towns in other counties. The success of this statewide campaign was demonstrated by a 227 percent increase in the distribution of toxin-antitoxin from 1924 to 1925 (Michigan State Board of Health, 1925-26).

Immunization efforts by the State Health Department continued into the 1930s. The activities were diverse and included (1) advising local health officers about prevalence and control of communicable disease, (2) providing advice regarding immunization campaigns and furnishing forms and literature, (3) distributing biologic products and (4) conducting research in biologic immunization (Michigan State Board of Health, 1936). In spite of these efforts, questions still remained as to why outbreaks of smallpox and diphtheria continued throughout the state. The Commissioner's Report in 1938 revealed this concern:

> It is not that our people are unconvinced of the value of protecting themselves against communicable disease. Men and women and children stand in line to be vaccinated,

> when there is a smallpox outbreak. The health problem is, how can such lineups be made obsolete and unnecessary? The feeling of some health workers is that our most difficult problems lie ahead, in bringing people to act as effectively in their own interest because of understanding and prudence as they do when they are afraid (Michigan State Board of Health, 1939, p. 12).

After 44 months of testing, a pertussis vaccine developed in Grand Rapids, Michigan was distributed to physicians throughout the state in 1940 (Michigan State Board of Health, 1940). Dissemination of immunization information was also emphasized during the year, including the distribution of a recommended immunization schedule agreed upon by the medical profession. In addition, immunization record cards accompanied by the recommended immunization schedules were given to the parents of newborn children along with birth certificates (Michigan State Board of Health, 1940).

In 1942 a number of special immunization programs were developed. First, an intense smallpox vaccination program was sponsored by the State Health Department. Its goal was 100 percent protection for infants 6-12 months; however, no results were reported on the success of this program (Michigan State Board of Health, 1942). The second major campaign involved an immunization program for Mexican migrants. Since these migratory workers were known to have a high incidence of diphtheria and low levels of protection against smallpox and diphtheria, the Michigan Medical Society together with county medical societies arranged an immunization schedule for children of these workers. It was noted that clinics were "strategically placed" in the sugar beet areas where the

Mexican migrants worked; approximately 5,000 individuals were vaccinated (Michigan State Board of Health, 1942).

A third immunization program was instituted nationwide by President Roosevelt in 1942. On February 6, a proclamation was issued recommending that all children should be immunized against diphtheria and smallpox by May 1, "as part of the national plan for defense" (Michigan State Board of Health, 1942, p. 227). The child welfare committee of the Michigan State Medical Society organized statewide programs through local medical societies and health departments. Instead of paying local physicians, token payments from federal funds were made to local medical societies participating in the program. An evaluation of this particular program is impossible due to the lack of data. A comment in the Annual Report of 1942 states that, "Progress reports indicate varying responses in the counties. An interesting outcome of the program has been the discovery of the high percentage of children in many areas who already had received the protective treatments" (Michigan State Board of Health, 1942, p. 227).

The number of immunizations administered by county, district and city health departments in the state generally increased during the 1940s. Between 1942 and 1943, however, there was a decrease in the number of smallpox, diphtheria and typhoid immunizations given for most age groups (Table 4). Attendance at public lectures and talks reportedly decreased as well. No explanation was provided but it is conjectured that World War II may have attracted attention

TABLE 4.--Immunizations Administered by County, District and City Health Departments in Michigan, 1941-1943.

	1941[a]	1942[b]	1943[c]
Smallpox - under 1 year	2,373	2,619	3,264
Smallpox - 1-4 years	8,838	13,625	12,026
Smallpox - 5 years and over	35,587	62,293	59,848
TOTAL	46,798	78,537	75,138
Diphtheria - under 1 year	2,748	3,819	4,102
Diphtheria - 1-4 years	9,917	16,597	13,337
Diphtheria - 5 years and over	17,450	37,039	31,657
TOTAL	30,115	57,455	49,096
Typhoid - complete immunization	742	1,761	701
Public lectures and talks	497	677	406
Attendance	14,908	19,160	14,457

SOURCES: [a]Michigan State Board of Health, Seventieth Annual Report, 1942, p. 212.

[b]Michigan State Board of Health, Seventy-First Annual Report, 1943, p. 116.

[c]Michigan State Board of Health, Seventy-Second Annual Report, 1944, p. 84.

away from immunization concerns and also may have disrupted the production and distribution of vaccines.

The importance of immunizations in Michigan was pointed out in terms of dramatic decreases in deaths from diphtheria. The state dropped from 954 deaths in 1921 to 12 deaths in 1951 (Michigan Department of Public Health, 1952). The need for continuing annual campaigns was noted, however, with an emphasis on immunizing children entering school for the first time. Although plans for immunization differed among communities, final responsibility was placed with the parents of each child.

By 1951, vaccines existed for diphtheria, whooping cough tetanus and smallpox (Michigan Department of Public Health, 1952). In addition, gamma globulin was available for the prevention and modification of measles (Michigan Department of Public Health, 1952). (It was first supplied by the American Red Cross in 1945-46.) The Michigan Department of Public Health urged parents to immunize their children as early as possible; three months was the recommended age for beginning immunizations. The use of the triple vaccine, DPT (Diphtheria-Pertussia-Tetanus), was encouraged as it was the most convenient method for both parents and physicians. The need for booster shots was also strongly emphasized as a means of acquiring lasting immunity (Michigan Department of Public Health, 1952).

The polio vaccine did not come into use until 1954. Polio has never been a particularly prevalent disease in the United States compared to smallpox, measles, and diphtheria. Approximately 1 out of every 1,000 persons in the population was struck with polio but

the paralysis caused by the disease made it one of the most feared (Reidman, 1974). The Salk vaccine underwent a massive public trial in April of 1954. Over 1.5 million children participated in the trial, along with 20,000 physicians and health officers, 40,000 nurses, thousands of teachers and a quarter of a million other volunteers. The results of the experiment showed that paralysis occurred six times more frequently in the unvaccinated children and that the vaccine was safe in 80-90 percent of the children (Reidman, 1974).

Once the Salk vaccine was formally announced as "safe, potent, and effective," millions of doses were distributed throughout Michigan. It was later learned, however, that several lots of vaccine accidentally contained the live virus, leaving over 200 people with polio and 11 people dead. Following this report, additional precautions were taken in the testing, mixing, and storage of the vaccine in order to restore the confidence of the public. It is not clear what effect this deadly mix-up had on the attitudes of the American public towards immunization, but in the summer of that same year (1954), millions of polio vaccinations continued to be administered across the country. By 1971, the number of polio cases in the United States had dropped from 18,304 in 1954 to only 17 (Reidman, 1974).

In spite of fewer reports of the childhood diseases discussed above, state health records indicate that there was continued concern among public health officials regarding the immunization status of residents throughout the 1960s. As the decade began,

citizens were reminded that 1,011 people in Michigan died and 42,465 persons became ill from 4 preventable diseases--polio, whooping cough, tetanus, and diphtheria (Michigan Department of Public Health, 1960). A national immunization survey carried out in the mid-1960s revealed some startling facts. Of children ages one to four, one-third had not completed the series of three DPT shots and 60 percent had not received the minimal four doses of polio vaccine (Table 5). In addition, one-third of adults between 20-29 years of age had not received even one dose of polio vaccine (Michigan Department of Public Health, 1964). Further analysis of survey results indicated that immunization status was lowest in lower socio-economic areas of cities. This finding prompted the flow of federal funds to finance several local immunization programs (Michigan Department of Public Health, 1965).

In this way, funds were finally obtained (in 1967) to purchase measles vaccine for distribution to local health departments in Michigan. Prior to this action, most local health departments had insufficient funds to offer the live virus vaccine licensed in 1963. A "Head Start" program in 1965 had provided some vaccine to children in low income groups but this program did not extend protection to most children throughout the state. In 1967, therefore, the school "Check Point" law became effective, thereby providing funds to buy enough vaccine to protect all children entering Michigan schools (Michigan Department of Public Health, 1967). Most of the funds were connected with the national campaign whose goal was the complete eradication of measles in the United States

TABLE 5.--Recommended Schedule for Active Immunization of Normal Infants and Children.

Age	Vaccine
2 months	DPT[a], TOPV[b]
4 months	DPT, TOPV
6 months	DPT, TOPV[c]
15 months	Measles, mumps, rubella, tuberculin test
18 months	DTP, TOPV
4- 6 years	DTP, TOPV
14-16 years	Td[d]; Repeat every 10 years

SOURCE: S. Krugman and S. L. Katz, "Childhood Immunization Procedures," JAMA, Vol. 237, No. 121 (1977), p. 2229.

[a]Diphtheria and tetanus toxoids combined with pertussis vaccine.

[b]Trivalent oral poliovirus vaccine.

[c]This dose is optional if polio is not endemic in the area.

[d]Tetanus and diphtheria toxoids (adult type) for those more than 6 years of age.

by the end of 1967. This national program established four essential concerns for success: (1) the routine immunization of all infants at the age of one, (2) immunization of all remaining susceptible children before entering public schools, (3) improved disease surveillance at all levels, and (4) immediate epidemic control at the first sign of an outbreak (Conrad et al., 1971).

Reasons for the failure of the above program have been proposed by Conrad et al. (1971) and by Riley (1976). Conrad et al. contend that the requirements established in the national program were simply not met with any degree of success. For example, the routine immunization of all one year olds, a key point of the program, failed to receive adequate funding. Just as various programs and campaigns for measles were starting, a national campaign for rubella was initiated; the measles program lost its priority as a federally funded project (Conrad et al., 1971). As a result, the 26,000 reported cases in 1969 jumped to 75,000 cases in 1971, directly attributable to the declining availability of the measles vaccine (Riley, 1976).

A result of this national interest was that the states were expected to use their revenue sharing funds for immunization programs. Most states, however, failed to use these funds for such purposes. A survey of state revenue sharing appropriations revealed that almost 11 percent of these funds was spent on road repairs, with approximately only 1 percent allocated for <u>all</u> health services (Riley, 1976).

The nation as a whole also failed to meet the other three requirements of the four-point program outlined above. Only 40 percent of all states and territories required measles immunizations for school entry as of 1970. Improvements in disease surveillance and reporting were also noticed in few areas, pointing to the need for better age-specific, epidemiologic data on all measles cases. Furthermore, numerous emergency requests for vaccines suggested that measles cases were not being adequately brought under control soon enough to prevent major outbreaks from occurring in schools and public institutions (Conrad et al., 1971).

In these ways, the development of immunization programs in the United States and in Michigan has expanded from the meager efforts of local physicians to massive state and national public campaigns. A reduction in disease case rates following the introduction of effective vaccines was a consistent and long-lasting trend for smallpox and diphtheria. The development of the measles vaccine, however, resulted in only temporary decreases in case rates of measles. An epidemiologic assessment of measles in the United States and in Michigan follows.

III. EPIDEMIOLOGIC ASPECTS OF MEASLES

Clinical Characteristics

Measles is an extremely contagious viral disease, transmitted by direct person-to-person contact or close physical proximity. It is endemic in all areas of the world except the most isolated populations. Measles is both a seasonal disease, usually occurring in late winter and early spring, and a periodic disease, recurring in two to three year epidemic cycles. Attack rates are usually highest among young children, peaking at six years of age in developed countries and two to three years of age in developing countries (Beeson and McDermott, 1971).

Symptoms of measles begin to appear after an 11-day (average) incubation period and consist of high fever, malaise, myalgia, headache, photophobia and conjunctivitis. Inflammation of the respiratory tract follows and laryngeal complications may also follow. The appearance of Koplik's spots on the buccal mucosa is a significant diagnostic feature as they often precede or overlap the development of a rash. The rash, which begins behind the ears or on the face, may spread downward to the trunk and extremities; it then fades approximately five days after onset (Beeson and McDermott, 1971).

Complications from measles usually stem from secondary bacterial infections. Otitis media (middle ear infection) and

pneumonia are the most common sequelae; however, the severity of complications is also greatly increased by conditions of overcrowding, malnutrition, and the prevalence of bacterial pathogens in the general population. Other complications may appear, including severe laryngitis, electrocardiographic abnormality, gastrointestinal problems, encephalomyelitis and giant-cell pneumonia. In addition, unfavorably modified measles, characterized by an atypical rash, may result from the administration of inactivated measles vaccine (Beeson and McDermott, 1971).

Mortality occurs in 1 out of every 10,000 cases in the United States. Encephalitis, creating the potential for brain damage and mental retardation, develops in 1 of every 1,000 cases. Roughly 1 out of every 100 cases results in pneumonia (Halpin et al., 1977).

No specific treatment for measles currently exists but immunity can be acquired in a number of ways. An attack of natural measles is considered the most effective way to achieve lifelong immunity. All infants up to six months of age, however, receive transient immunity by placentally transferred maternal antibodies. Immunization can also occur with the administration of gamma globulin (temporary), live virus vaccine with standardized immune globulin, or live further attenuated virus vaccine (Beeson and McDermott, 1971).

The Diffusion Process

The balance of immune and susceptible persons in the population is very crucial to the spread of measles. The exact proportion of susceptibles needed to sustain an epidemic has been subject to debate, however. Studies during the early part of the 1900s found that urban areas were protected from epidemics when the level of immunity in the population was greater than 55 percent (Sencer et al., 1967). Thus, the concept of herd immunity was developed. Epidemic outbreaks of measles in the 1970s, however, have been reported in populations with immunity levels as high as 85 percent (Schiff et al., 1975) and 89 percent (Wyll and Witte, 1971). Dittman et al. (1976) found that measles could be eradicated in a community only when 90 percent of the susceptible population was immunized. Cherry et al. (1972) suggest that the spread of the virus depends not only on the number of susceptibles in a population but also on their opportunities for contact.

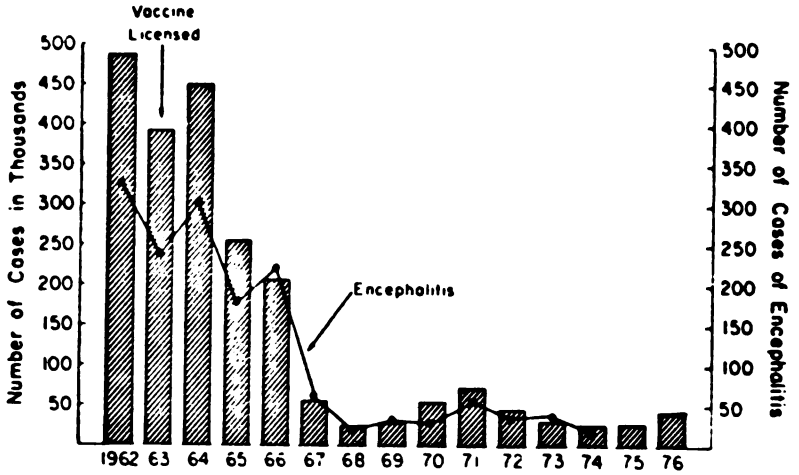
Modes of spread can be measured in a number of ways. One method involves the use of planar graph techniques which can be used to analyze different spatial processes at different stages of an epidemic (Haggett, 1976). In a study of 2 epidemic waves over a 222-week period, Haggett plotted measles cases in 28 administrative areas. The join-count measure of spatial autocorrelation was used to determine degrees of clustering or separation present during various stages of the epidemics. Patterns of spatial contagion were analyzed by viewing planar graphs based on seven different models of disease diffusion: (1) regional, (2) urban-rural,

(3) local contagion, (4) wave contagion, (5) journey-to-work, (6) population size, and (7) population density. Analysis of the graphs showed that (1) during endemic periods infections persisted in larger population clusters and moved slowly through low density rural areas in a sporadic manner, (2) during the advanced phase of the epidemic the influence of population size on spread decreased and the wave effect became much more important, and (3) at the peak of the epidemic wave local contagion was an important factor in the spread of the virus. In addition, the impact of successful vaccination programs could be determined by the lack of distinct advance and retreat phases usually displayed by a classic epidemic wave. In this way, various geographic methodologies can thus be used to predict the spread of epidemic diseases and can also be used to evaluate the impact of immunization programs on the spread of those diseases. More specific suggestions for applying geographic methodologies to disease control problems are discussed in Section V.

The Current Status of Measles in the United States

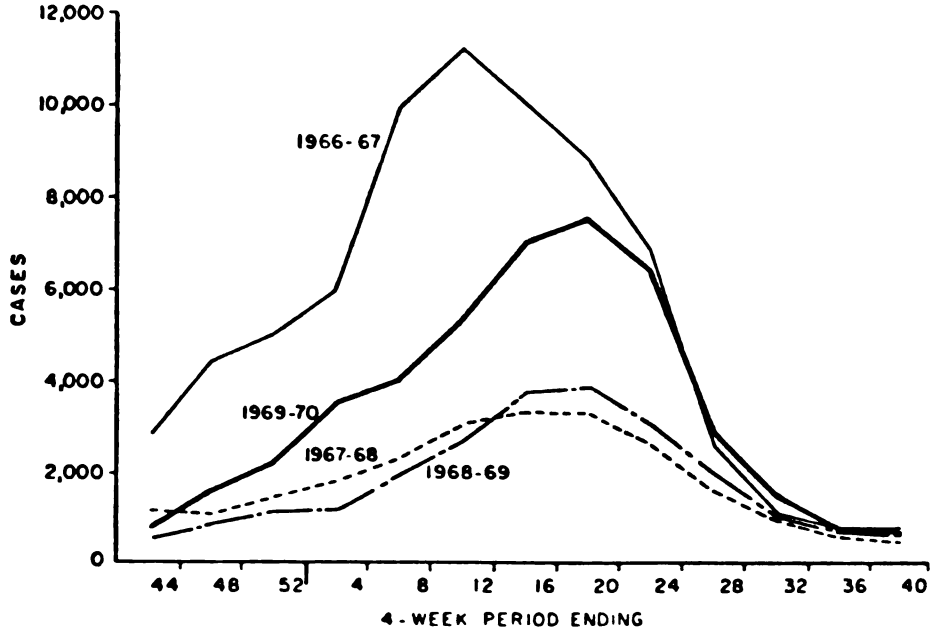
Vaccine licensure has had a profound effect on the epidemiology of measles in the United States. The number of measles cases dropped over 90 percent from 1963 to 1968, followed by a corresponding decrease in cases of post measles encephalitis (Figure 1).

Since 1969, as mentioned above, a resurgence of measles has been evident (Figure 2). An investigation of measles morbidity from epidemologic year 1968-69 to 1969-70, revealed increases in



SOURCE: Saul Krugman, "Present Status of Measles and Rubella Immunization in the United States: A Medical Progress Report," Journal of Pediatrics, Vol. 90, No. 1 (1977), p. 2 (reprinted with permission).

Figure 1.--Number of reported cases of measles and measles encephalitis in the United States, 1962-1976.

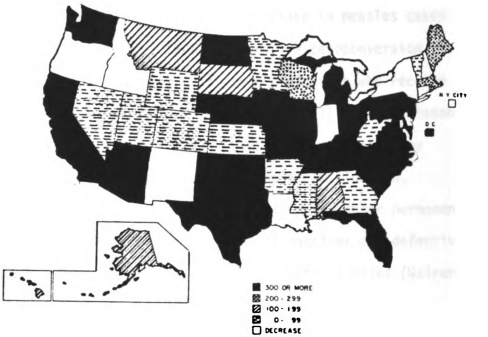


SOURCE: J. L. Conrad et al., "The Epidemiologic Rationale for the Failure to Eradicate Measles in the United States," American Journal of Public Health, Vol. 61, No. 11 (1971), p. 2306 (reprinted with permission).

Figure 2.--Reported cases of measles by 4-week period USA, epidemiologic year 1969-70 compared with 1966-67, 1967-68, and 1968-69.

41 states, decreases in 9 states and New York City, and no change in only 1 state (Vermont) (Figure 3). A total of 21,210 new cases were reported for the epidemiologic year 1969-70, with an average increase of 90 percent, for all 50 states over the previous year (Conrad et al., 1971).

One particular concern associated with this recent resurgence has been the occurrence of measles in previously vaccinated children. The most prominent reason given for this phenomenon seems to be related to the age at which vaccinations are administered. For instance, Cherry et al. (1972) found that the average attack rate for children vaccinated under age one was 6.2 percent, compared to an average attack rate of 1.7 percent for those vaccinated during or after their first birthday. Cherry et al. also discovered that 50 percent of the vaccine failures reported occurred in children vaccinated before the age of one. Another study from Birmingham, Alabama (Currier et al., 1972) revealed even more startling results. Of a total of 37 measles cases reported during an epidemic, 25, or 68 percent, of the children had received live further attenuated virus vaccine. Further investigation of the victims revealed that the attack rate for those immunized at less than 12 months of age was 17.6 percent while those immunized after 12 months of age had an attack rate of 1.9 percent. This difference was significant at $p < .01$. In this study, the occurrence of measles in vaccinated children was attributed to possible overdosages of measles immune globulin during immunization and to the



SOURCE: J. L. Conrad et al., "The Epidemiologic Rationale for the Failure to Eradicate Measles in the United States," American Journal of Public Health, Vol. 61, No. 11 (1971), p. 2308 (reprinted with permission).

Figure 3.--States showing increase or decrease of measles cases for epidemiologic year 1969-70 over the epidemiologic year 1968-69.

presence of maternal antibodies in children vaccinated under 12 months of age.

Several other explanations for the rise in measles cases have been suggested as well. One concerns the seroconversion failure rate which occurs in 3 to 5 percent of those who receive the live attenuated vaccine (Wyll and Witte, 1971). Other reasons include the administration of killed measles virus vaccine by itself and passive immunization with immune serum globulin, techniques which are noted for their inability to confer permanent immunity. Improper handling and storage of vaccines and defective batches of vaccines are cited as additional possibilities (Weiner et al., 1977).

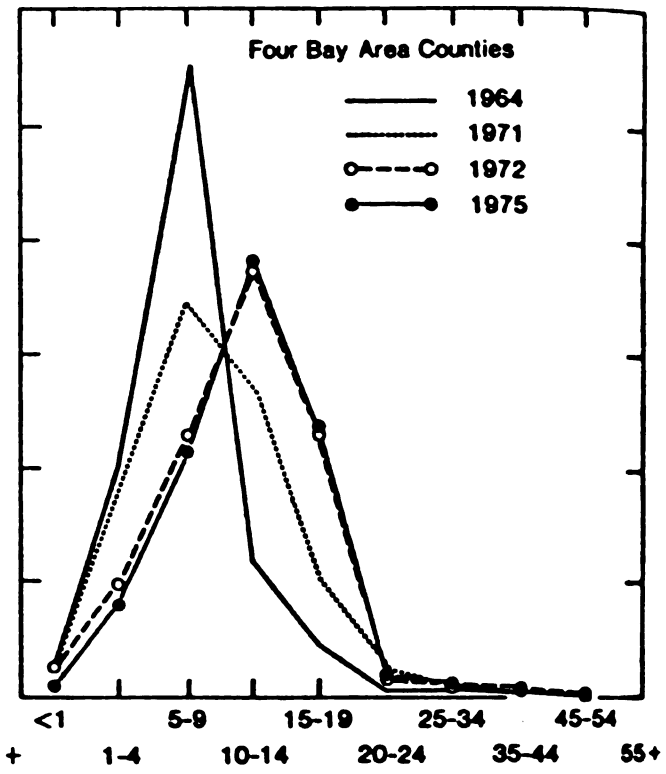
A major problem associated with the phenomenon of unsuccessful immunization is that many people who think they are adequately immunized are actually at risk to contracting measles. This condition has resulted in outbreaks among large numbers of adolescents and young adults throughout the United States. For example, an outbreak in New York involved 12-19 year old students in junior and senior high schools, an unusual departure from past epidemiologic trends (Weiner et al., 1977). Similarly, an investigation of an epidemic in Ohio revealed that the majority of measles cases occurred in children 10-14 years of age (Halpin et al., 1977).

A study of the changing distribution of measles among different age groups was conducted in California by Rand et al. (1976). This study revealed a definite decrease over time in the percentage of cases among the five to nine year old age group and a consequent

increase in the 10-14 and 15-19 year old age groups (Figure 4). A comparison of the total number of measles cases and age-specific case rates from 1964 to 1975 in the San Francisco Bay area revealed a declining attack rate for all previously vaccinated age groups except the 10-14 and 15-19 year old age groups. Rand et al. suggest that the lack of a statewide immunization policy until 1964 and the lack of uniform standards and regimens may be responsible for a large population of inadequately vaccinated adolescents and young adults.

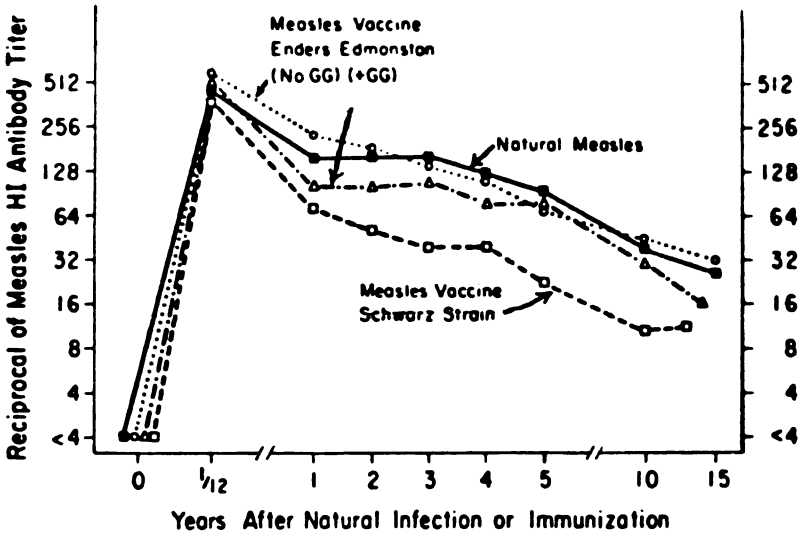
In general immunity induced by live further attenuated vaccine is apparently long-lasting. Prospective studies of children immunized in four different ways indicate that antibody responses continue to be similar following natural infection and vaccination after 15 years (Krugman, 1977). Geometric mean titers of antibody response were found to be highest after natural infection or Edmonston B vaccine, intermediate following gamma globulin (GG) with Edmonston B vaccine and lowest after immunization with further attenuated measles-virus vaccine, Schwartz strain (Figure 5).

Age is considered an important factor in vaccine failures. It has been suggested that measles immunization be delayed until 15 months of age (Krugman, 1977). Reimmunization of those who experienced initial vaccine failures is also recommended. Krugman (1977) contends that no evidence has been found to support the idea that subacute sclerosing panencephalitis is associated with the vaccination of immune persons. Furthermore, the risk of central nervous system complication is much greater following natural



SOURCE: K. H. Rand et al., "Measles in Adults: An Unforeseen Consequence of Immunization?" JAMA, Vol. 236, No. 9 (1976), p. 1030 (reprinted with permission). Copyright 1970, American Medical Association.

Figure 4.--Changing measles incidence among age groups in San Francisco, 1964-1975.



SOURCE: Saul Krugman, "Present Status of Measles and Rubella Immunization in the United States: A Medical Progress Report," Journal of Pediatrics, Vol. 90, No. 1 (1977), p. 3 (reprinted with permission).

Figure 5.--Measles antibody response and persistence after natural infection and immunization: a 15-year follow-up.

infection than following vaccination. Even though vaccine failure is a factor in the changing epidemiology of measles within the last decade, most measles cases have occurred in unimmunized children. A susceptible population of five million (children and adolescents) still exists and this is a large enough reservoir to sustain periodic outbreaks of measles (Krugman, 1977).

Although measles can be found in all societies, its incidence is not evenly distributed throughout the United States. The more frequent occurrence of measles among lower socio-economic groups has been noted in numerous studies. In Landrigan and Conrad's study (1971), 87 percent of measles patients in Los Angeles County were from lower and lower-middle socio-economic groups. Schiff et al. (1975) noted during their investigation of rubella and measles that Indian children of low socio-economic status showed a lower susceptibility rate of measles than middle class children; this finding suggests that lower income populations are more likely to develop immunity at an earlier age by natural infection. Pyle's (1973) investigation of a measles epidemic in Akron, Ohio revealed that socio-economic status affected the spread of measles through the city. Using cartographic analysis techniques to examine the distribution and spread of measles cases, he found that the poorest areas in the city experienced the most severe and most long-lasting epidemic waves. A correlation analysis of 12 socio-economic variables revealed that income and education had the highest negative correlation with measles, -0.643 and -0.606, respectively.

The distribution of measles cases also varies among ethnic groups in the United States. A survey of measles in Dallas County, Texas, in which 17 percent of the total population was black, revealed that a disproportionate number, over 50 percent, of the measles patients were black (Landrigan and Conrad, 1971). Similarly, during an epidemic in Birmingham, Alabama, 76 percent of the cases occurred in black children; the disease was distributed in four lower socio-economic areas of the city which were predominantly black (Currier et al., 1972). Pyle (1973) also found that areas in Akron with proportionately large black populations, usually located in the inner city, reported the highest attack rates. He reported a value of 0.583 for the correlation of "percent negro" with measles (Pyle, 1973). Although this correlation is not as strong as that of income and measles, these two variables are strongly interrelated. The higher rates among the black population are no doubt a reflection of income and socio-economic status.

Contrasts in the characteristics of measles between urban and rural areas have also been noted. Landrigan and Conrad (1971) found that in urban outbreaks most cases (53 percent) occurred among preschoolers (ages one to four), whereas the suburban and rural areas reported the majority of cases (61 percent) among children five to nine years old. This difference was attributed to the earlier age of mingling in nursery schools and day care centers in cities. Similar findings were reported by Cherry et al. (1972) in their study of measles in St. Louis City and St. Louis County. Attack rates for children up to four years old within the city limits were nearly

double those of the five to nine year olds. Within that county, however, attack rates for children five to nine years old was more than four times that of children four years old and under.

In addition to urban-rural differences, other regional variations are evident throughout the United States. The existence of a regional concentration of measles cases was first reported by Landrigan and Conrad (1971) who noted that the greatest concentration was in the East North Central states. Although major increases have been reported throughout the country since the early 1970s, the East North Central states have reported the largest percentage increase in cases of measles in the latter part of the decade. For example, from 1975 to 1976 Ohio reported a 584 percent rise in measles incidence, compared to a 64 percent increase for the nation as a whole (Halpin et al., 1977). As of March 1977, nationwide reporting was running twice as high as in 1976 and the East North Central states were once again showing the highest increases (Halpin et al., 1977). The most noteworthy increase in this region was reported in Michigan which reported approximately one-third of the nation's total measles cases (over 8,000) in 1978 (Center for Disease Control, 1979). Since Michigan is representative of a high-risk area for measles within the United States, epidemiologic aspects of measles in this state are examined next.

The Status of Measles in Michigan

Michigan's experience with measles since the turn of the century parallels that of the nation as a whole. In general, case

rates have been quite high and the two to three year epidemic cycle has been evident until 1966 (Table 6). Between 1935 and 1942, exceptionally high case rates were reported in 1935, 1938, and 1941 compared to 1936, 1937, 1939, 1940 and 1942; this pattern indicates that epidemics were occurring every three years. Alternating two and three year epidemic waves of measles occurred up until 1966 when the measles vaccine became available to Michigan residents. A sharp decrease in case rates occurred after 1966, dropping from 183.4 per 1000,000 in 1966 to 12.2 per 100,000 in 1965 (Michigan Department of Public Health, Office of Vital and Health Statistics, 1978).

Measles incidence continued to decline until 1969, when a slight increase in the number of cases was first reported. A major change occurred in 1970 when the number of cases increased over 400 percent from the previous year. From 1970 through 1978, the two to three year epidemic cycle has become further evident, indicating that a large susceptible population still exists in Michigan (Michigan Department of Public Health, 1978).

The sharp increase in the number of cases reported for 1978 is not only high compared to previous years within Michigan but is also approximately three times higher than the number of cases reported by any other state in the country (Table 7). The East North Central states accounted for nearly half of all the measles cases in 1978. Furthermore, 70 percent of those cases in East North Central states occurred in Michigan (Center for Disease Control, 1979).

TABLE 6.--Number of Measles Cases and Case Rates in Michigan, 1900-1978.

Year	Number of Cases	Case Rates per 100,000	Year	Number of Cases	Case Rates per 100,000
1900	20,356	840.8	1940	20,206	384.4
1901	4,629	188.2	1941	70,748	1,301.1
1902	11,978	479.3	1942	8,569	154.7
1903	8,941	352.3	1943	51,764	962.6
1904	10,386	403.1	1944	26,711	496.7
1905	6,061	231.7	1945	6,328	116.4
1906	7,403	278.9	1946	42,261	740.3
1907	12,139	450.7	1947	9,574	157.8
1908	4,775	174.8	1948	42,952	693.3
1909	9,047	326.5	1949	20,279	319.3
1910	13,934	495.8	1950	38,245	600.2
1911	9,639	332.8	1951	15,227	232.7
1912	2,834	95.0	1952	32,941	491.1
1913	9,185	299.4	1953	23,334	340.5
1914	11,356	360.1	1954	40,725	579.8
1915	4,438	137.0	1955	23,882	330.0
1916	12,143	365.2	1956	41,966	558.4
1917	14,472	424.3	1957	19,070	244.4
1918	6,726	192.4	1958	41,448	526.9
1919	8,885	248.0	1959	12,234	153.7
1920	22,364	609.6	1960	36,161	462.2
1921	3,043	80.4	1961	29,391	371.9
1922	12,107	310.2	1962	25,303	318.7
1923	30,041	747.2	1963	48,752	607.1
1924	18,290	442.0	1964	30,897	381.4
1925	10,332	242.8	1965	28,132	343.1
1926	39,946	913.5	*1966	15,251	183.4
1927	8,303	184.9	1967	1,048	12.2
1928	27,039	586.9	1968	353	4.1
1929	18,040	381.8	1969	401	4.6
1930	28,129	580.9	1970	1,834	20.7
1931	6,212	127.2	1971	2,659	29.6
1932	42,129	855.4	1972	2,353	26.1
1933	21,654	436.0	1973	4,552	50.2
1934	6,528	130.4	1974	2,365	26.0
1935	79,061	1,565.8	1975	3,253	35.5
1936	2,453	48.2	1976	6,139	67.4
1937	6,154	119.9	1977	1,392	15.2
1938	79,400	1,534.8	1978	8,006	87.7
1939	12,948	248.3			

SOURCE: Michigan Department of Public Health, Vital and Health Statistics, 1978 Michigan Health Statistics.

*Measles vaccine distributed in Michigan.

TABLE 7.--Cases of Measles by Geographic Area in the United States, 1978.

Reporting Area	No. of Cases	Reporting Area	No. of Cases
UNITED STATES	26,795	EAST SOUTH CENTRAL	1,440
NEW ENGLAND	2,057	Kentucky	122
Maine	1,319	Tennessee	966
New Hampshire	86	Alabama	102
Vermont	53	Mississippi	250
Massachusetts	263		
Rhode Island	8	WEST SOUTH CENTRAL	1,453
Connecticut	328	Arkansas	16
		Louisiana	385
MID-ATLANTIC	2,281	Oklahoma	19
Upstate New York	1,438	Texas	1,033
New York City	405		
New Jersey	75	MOUNTAIN	266
Pennsylvania	363	Montana	107
		Idaho	1
EAST NORTH CENTRAL	11,587	Wyoming	-
Ohio	497	Colorado	37
Indiana	234	New Mexico	-
Illinois	1,335	Arizona	57
*Michigan	8,006	Utah	44
Wisconsin	1,515	Nevada	20
WEST NORTH CENTRAL	602	PACIFIC	1,624
Minnesota	43	Washington	438
Iowa	76	Oregon	529
Missouri	173	California	654
North Dakota	211	Alaska	1
South Dakota	---	Hawaii	12
Nebraska	5		
Kansas	94	Guam	25
		Puerto Rico	315
SOUTH ATLANTIC	5,485	Virgin Islands	6
Delaware	7	Pacific Trust	
Maryland	51	Territories	650
District of Columbia	2		
Virginia	2,836		
West Virginia	1,068		
North Carolina	125		
South Carolina	199		
Georgia	36		
Florida	1,161		

SOURCE: Center for Disease Control, "Cases of Specified Notifiable Diseases: United States," Morbidity and Mortality Weekly Report, January 5, 1979, p. 532.

Within Michigan in 1978, Wayne County reported the highest incidence (1,000 cases) but a fairly low crude morbidity rate (41 per 1000,000 population) compared to the rest of the state (Michigan Department of Public Health, 1978). Ingham County, on the other hand, reported nearly as many cases as Wayne County; the county's crude morbidity rate was 309 per 100,000. The drastic increase in cases reported in Ingham County from 1977 to 1978 compared to those from Wayne County and the city of Detroit are shown in Table 8.

The city of Detroit surprisingly shows, according to Table 8, a decrease in cases between 1976 and 1977 and only a slight increase from 1977 to 1978. Since previous studies have indicated that higher attack rates occur among black populations and those of lower socio-economic status, one would expect much higher disease rates than those reported for Detroit, which has a large black population and a large population in the lower socio-economic classes. A school immunization law which went into effect in Detroit in 1976 is no doubt a reflection of its enforcement and the low incidence for 1978 (see Section IV).

Two major groups in Michigan were affected by the measles epidemic in 1978. One was children in the upper grades, ages 10-15 years; this group accounted for most of the measles morbidity during the epidemic season. Morbidity was believed to be attributed to ineffective immunization among these children, either because of inactivated vaccines received or vaccines administered before age one (Simonsen, 1978). The second major group affected was

TABLE 8.--Measles Cases in Selected Locations, 1976-1978.

Location	Number of Cases		
	1976	1977	1978
Ingham County	10	4	840
Wayne County	264	97	1,000
Detroit	526	417	465

SOURCE: Michigan Department of Public Health, Bureau of Disease Control and Laboratory Services, Division of Epidemiology, Weekly Surveillance Report, 52nd Week, 1976, 1977, 1978.

preschoolers. Measles among this segment of the population is considered important because hospitalization rates among two year olds are much higher than among those ten years of age (Simonsen, 1978).

One investigation which began in November 1978 attempted to examine certain epidemiologic features of measles cases in Michigan from the 1977-78 epidemic season (Bernier et al., 1978). For example, 1 death from a case of atypical measles was uncovered, in addition to 1 case of encephalitis, 50 hospitalizations and 13 cases of pneumonia. One useful finding evolved from an investigation into the cases reported as measles. A sample of 225 cases from Michigan and 160 cases from Detroit were analyzed for whether or not they met the standard Center for Disease Control case definition of measles. A case was designated "measles" if it met three criteria: (1) fever $\geq$ 101° F., or "high"; plus (2) rash duration $\geq$ 3 days; plus (3) cough, coryza, or conjunctivitis. Of the sample cases counted as measles, 20 percent of Michigan's cases and 9 percent of Detroit's cases failed to meet the standard case definition; that is, there was apparently a significant amount of overreporting. This overreporting was supposedly due to a variety of different case report forms used throughout the state and the lack of a standard by which to define and judge measles cases (Bernier et al., 1978).

Another significant finding of this Michigan investigation was that most of the cases occurred in children ages 15 months to 18 years with undocumented, unknown, or no vaccination history, and not among adequately vaccinated persons as had been thought.

Twenty-five percent of the cases in Michigan and 36 percent of the cases in Detroit occurred among those with a documented vaccination history; that is, defined as having at least the month and year of vaccination recorded or having a written vaccination record examined by an investigator (Table 9). Still, 69 percent of Michigan's cases were considered preventable. The conclusion of Bernier et al. (1978, p. 18) was that, "Identification and vaccination of those children (including revaccination of those who cannot document a previous vaccination) should have prevented their illness."

A statewide study of measles reporting systems was also conducted in 1978 (Bernier et al., 1978). A survey of 43 counties in the state plus Detroit revealed that 3 of the counties had no school reporting system, 8 counties reported no verification system and 4 counties reported neither a school reporting system nor a case verification system. Based on previous experience, school systems with no verification system are accurate in only one out of every two or three cases reported. By applying this estimate of verification to counties with no case verification system, a corrected estimate of measles cases for the state was reduced to 76.4 percent of the original estimate. Furthermore, a corrected measles incidence for Michigan was changed from 297 cases per 100,000 population under 18 years old (as of week 47 in 1978) to 227. Even with the corrected incidence, the state still ranked second highest (behind Maine) in the nation's rate of measles cases (Bernier et al., 1978). Bernier et al. (1978, p. 26) concluded that even though 24 percent of the measles cases reported in Michigan were false

TABLE 9.--Vaccination Status of Sampled Measles Cases* by Area.

Vaccination Status	Detroit Sample N = 134		Michigan State Sample N = 159	
	No.	%	No.	%
Documented (Written Record)	48	(35.8)	39	(24.5)
Undocumented (Verbal Response)	53	(39.6)	66	(41.5)
No Vaccination	33	(24.6)	54	(34.0)

SOURCE: Roger Bernier et al., "Trip Report: Michigan, November 27-December 1, 1978," p. 15.

*Cases include those meeting the case definition and those considered possibly measles.

positives, "Michigan's high measles incidence rate cannot be explained away merely as an artifact of a sensitive but not very specific reporting system."

Spatial Aspects of Measles in Michigan

In order to determine the magnitude of Michigan's reservoir of susceptibles which was responsible for perpetuating the high incidence rates of measles, immunization reports from Michigan's 83 counties were examined. The most complete records of immunity levels that currently exist are the new school entrants immunization reports, which are somewhat complete for the school years 1976-1977, 1977-1978 and 1978-1979. Criteria for complete immunization was slightly different for each school year. Immunization was considered complete for the school years 1976-1977 and 1977-1978 when a child had received: (1) at least three DPT shots (four were required in 1976-1977), (2) at least three polio shots, (3) one measles shot, and (4) one rubella shot. For the school year 1978-1979, immunization was not considered complete until a child had received all of the above plus one mumps shot.

The percentages of incompletely immunized new school entrants for each county were ranked and divided into quartiles for each school year. Quartiles were used so that 25 percent of the counties with the highest susceptible populations would stand out as target areas. The percentages of susceptible populations for each county for the school years 1976-1977 through 1978-1979

are shown in Figures 6a, 7a and 8a. The spatial distributions of susceptible populations, based on quartile divisions of the data, are shown in Figures 6b, 7b and 8b.

Examination of incompletely immunized children entering Michigan schools for the first time reveals that there is indeed a large reservoir of susceptibles capable of sustaining epidemic outbreaks in the state. From 1976-1977 to 1978-1979 the proportions of susceptible school entrants on a statewide basis increased from 12 percent in 1976-1977 to 25 percent in 1977-1978, and reached 31 percent in 1978-1979. The highest percentage of susceptibles reported by a single county in 1976-1977 was 48 percent (Alpena County). In 1977-1978 the highest percentage reported was 41 percent (Delta County) and in 1978-1979 it was up to 60 percent (Lake County). Counties reporting complete immunization for 100 percent of their school entrants included Keweenaw County and Alger County in 1976-1977 and only Keweenaw County in 1978-1979. As mentioned above, epidemics can occur in a population in which only 11 percent are susceptibles (Wyll and Witte, 1971). Thus, many of the counties in Michigan could be considered high-risk epidemic areas during the time periods under consideration.

Interpretation of the spatial distribution of susceptible populations in Michigan from 1976-1977 to 1978-1979 is complicated by several factors. First, the increasing levels of suceptible populations from 1976-1977 to 1978-1979 may be an artifact of confusion caused by a change in reporting forms for each school year. Secondly, the differences in criteria for the three time periods

SOURCE: Michigan Department of Public Health, "New School Enterers Immunization Status Report by County, 1976-77."

Figure 6a.--Percentage of susceptible school entrants by county, 1976-1977.

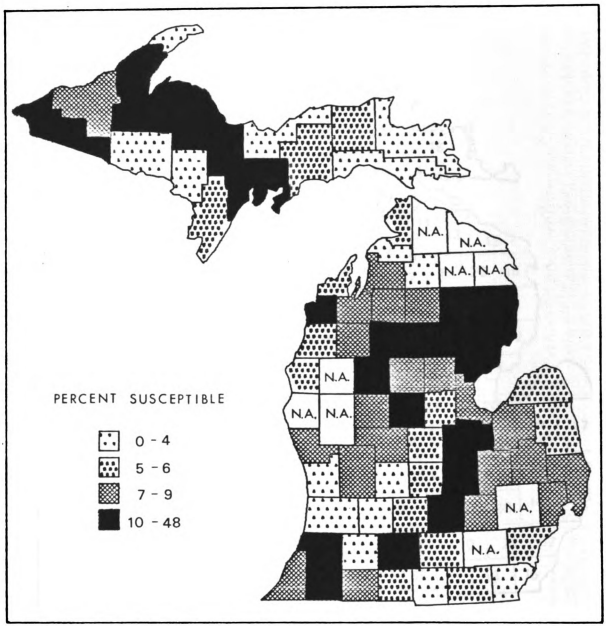
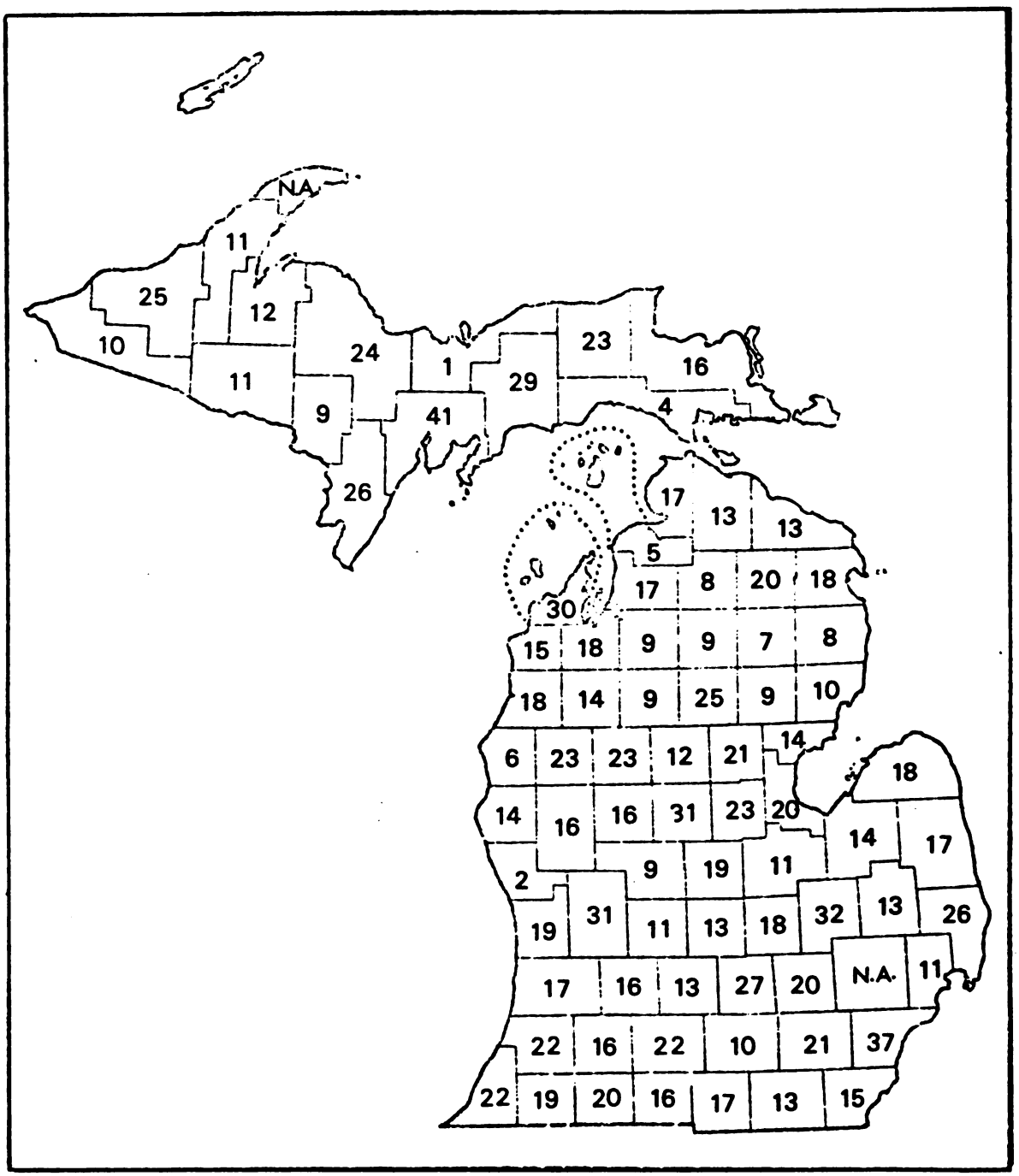


Figure 6b.--Quartile distribution of susceptible school entrants, 1976-1977.



SOURCE: Michigan Department of Public Health, "Percentage of New Entrants Immunized, 1977-78."

Figure 7a.--Percentage of susceptible school entrants by county, 1977-78.

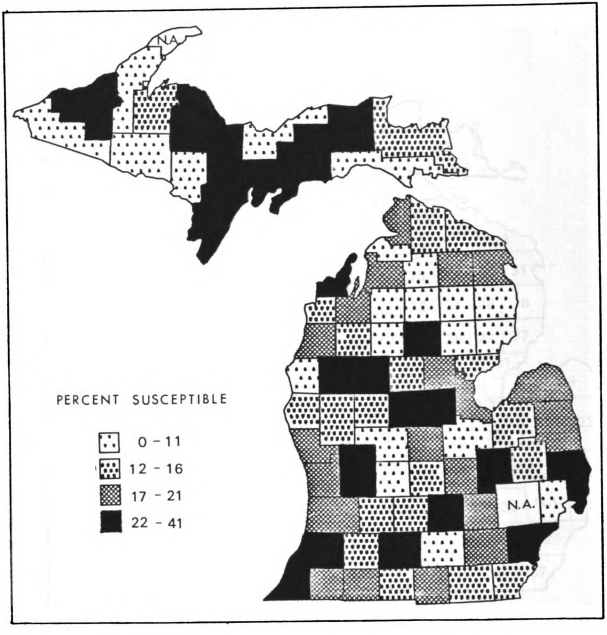


Figure 7b.--Quartile distribution of susceptible school entrants, 1977-1978.

SOURCE: Michigan Department of Public Health, "Michigan New School Entrants Immunization Report, 1978-1979."

Figure 8a.--Percentage of susceptible school entrants by county, 1978-1979.

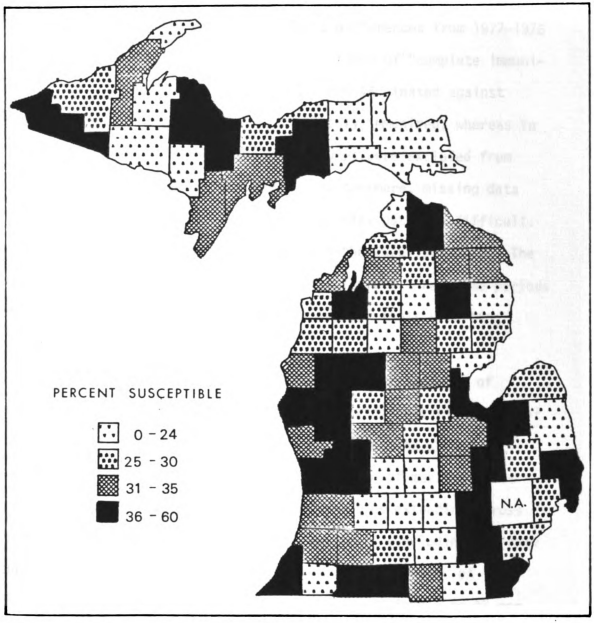


Figure 8b.--Quartile distribution of susceptible school entrants, 1978-1979.

affected the immunization reports. Between 1976-1977 and 1977-1978 in order to be counted as "completely immunized," parents of the school children had to present documentation stating the dates of each vaccination (Simonsen, 1978). Thus, differences from 1977-1978 to 1978-1979 may be due to changing definitions of "complete immunization" during these three years. Those not vaccinated against mumps in 1977-1978 were counted as completely immunized, whereas in 1978-1979, those not vaccinated against mumps were excluded from those counted as completely immunized. Furthermore, missing data from several counties makes analysis of spatial patterns difficult. This problem is particularly noticeable in the 1976-1977 data. The lack of available data from Oakland County for all three time periods suggests that efforts should be made to improve their reporting system.

With these considerations in mind, spatial analysis of unimmunized school children in Michigan indicates that clustering of large susceptible populations may have encouraged the spread of measles that resulted in the unusually high rate of measles cases in 1978. Figure 6b shows that a band of counties extending across the northern part of the western upper peninsula (excluding Keweenaw County) and a group of counties in the north central part of the lower peninsula contained susceptible populations from 7 to 48 percent. By 1977-1978, the range in the percentage of susceptibles nearly doubled and the counties with the highest percentage of susceptibles had changed (Figure 7b). In the upper peninsula, the high-risk areas shifted to the east and in the lower peninsula, most

of the counties in the north central section that were in the highest quartile of susceptibles in 1976-1977 were in the lowest quartile of susceptibles in 1977-1978. The cluster of high-risk counties that extended south from the Saginaw Bay area in 1976-1977 was dispersed in 1977-1978, resulting in a scattering of target areas with no clear consistent pattern (Figure 7b). For the 1978-1979 school year, high-risk counties once again showed a somewhat clustered pattern (Figure 8b). A north-south line of counties extending from Bay County to Monroe County reported extremely high susceptible populations, ranging from 36 to 60 percent. Another cluster of high-risk counties, with susceptible populations ranging from 31 to 60 percent, existed along the western boundary of the state. The only county that remained in the highest quartile all three years was Marquette County.

These data show that pockets of large susceptible populations existed in Michigan from 1976 through 1979. Large increases or decreases in immunity levels within counties between 1976-1977 and 1978-1979 could be the result of several factors. The diffusion of an epidemic wave through a county can infect, and therefore render immune, large numbers of susceptibles; the level of susceptibility is reduced until, through additional births, the susceptible population reaches critical levels again. Significant changes in the level of susceptibility within a county can also occur through immunization campaigns. From the data presented here it is impossible to explain changes in the levels of susceptibility. Further investigation at smaller scales is therefore suggested. A county

such as Osgoda, whose percentage of susceptibles changed from 48 (1976-1977) to 7 (1977-1978) to 38 (1978-1979), should be studied in further detail; examination of measles cases reports and vaccine dosages administered in the county could be an initial step of the investigation.

Implementation of better reporting systems and spatial analysis of immunity levels throughout Michigan could possibly have presented the spread of measles which resulted in over 8,000 cases in 1978. Greater use of spatial analytical techniques to predict potential epidemic outbreaks and prevent diffusion into other areas could be very beneficial to health care planners and epidemiologists. A discussion of various control methods follows.

IV. PREVENTION AND CONTROL PROGRAMS

The need for more effective disease control measures has been a rising concern since the resurgence of measles in the United States became evident. Although eradication attempts failed in the late 1960s, efforts towards this goal were further emphasized in the late 1970s. The Carter Administration stated two objectives concerning the control of measles: (1) to raise the immunization level of preventable childhood diseases to over 90 percent by October 1, 1979 and (2) to eliminate indigenous measles from the United States by 1982 (Califano, 1978). This section examines the cost-effectiveness of immunization programs and reviews some specific control programs that have been successful in improving immunization levels and in preventing epidemic outbreaks of measles. A review of the current status of immunization programs in Michigan is also included.

Cost-Effectiveness of Immunization Programs

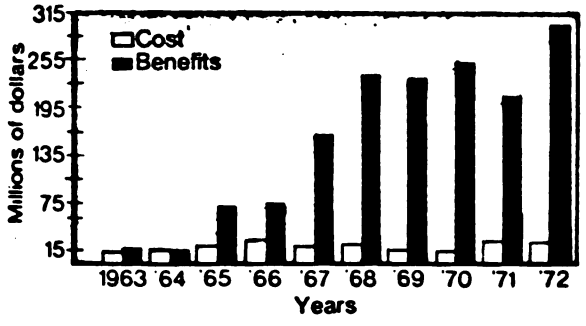
Cost-benefit analyses have demonstrated that immunization control programs are cost-effective. Witte and Axnick (1975) examined examined both humanistic and economic benefits in relation to costs of measles immunization from 1963 to 1972. During that decade an estimated 24 million cases and 2,400 deaths from measles were averted. Other types of savings included 8,000 cases of mental retardation that were prevented, 78 million school days saved,

12 million physician visits avoided, and 1 million hospital days saved. The economic costs of immunization during this same period were relatively stable in relation to the benefits achieved (Figure 9). Total costs included vaccine production, distribution, administration and promotional expenses. The net economic benefits for ten years were valued at 1.3 billion dollars. According to Joseph Califano, former Secretary of the Department of Health, Education and Welfare, this monetary estimate should be even higher. He stated that the United States has received ten dollars in benefits for every one dollar the federal government invested in immunizations against measles, resulting in a savings of two billion dollars (Califano, 1978). Components of some of these immunization programs are discussed below.

Examples of Successful Approaches to Immunization in the United States

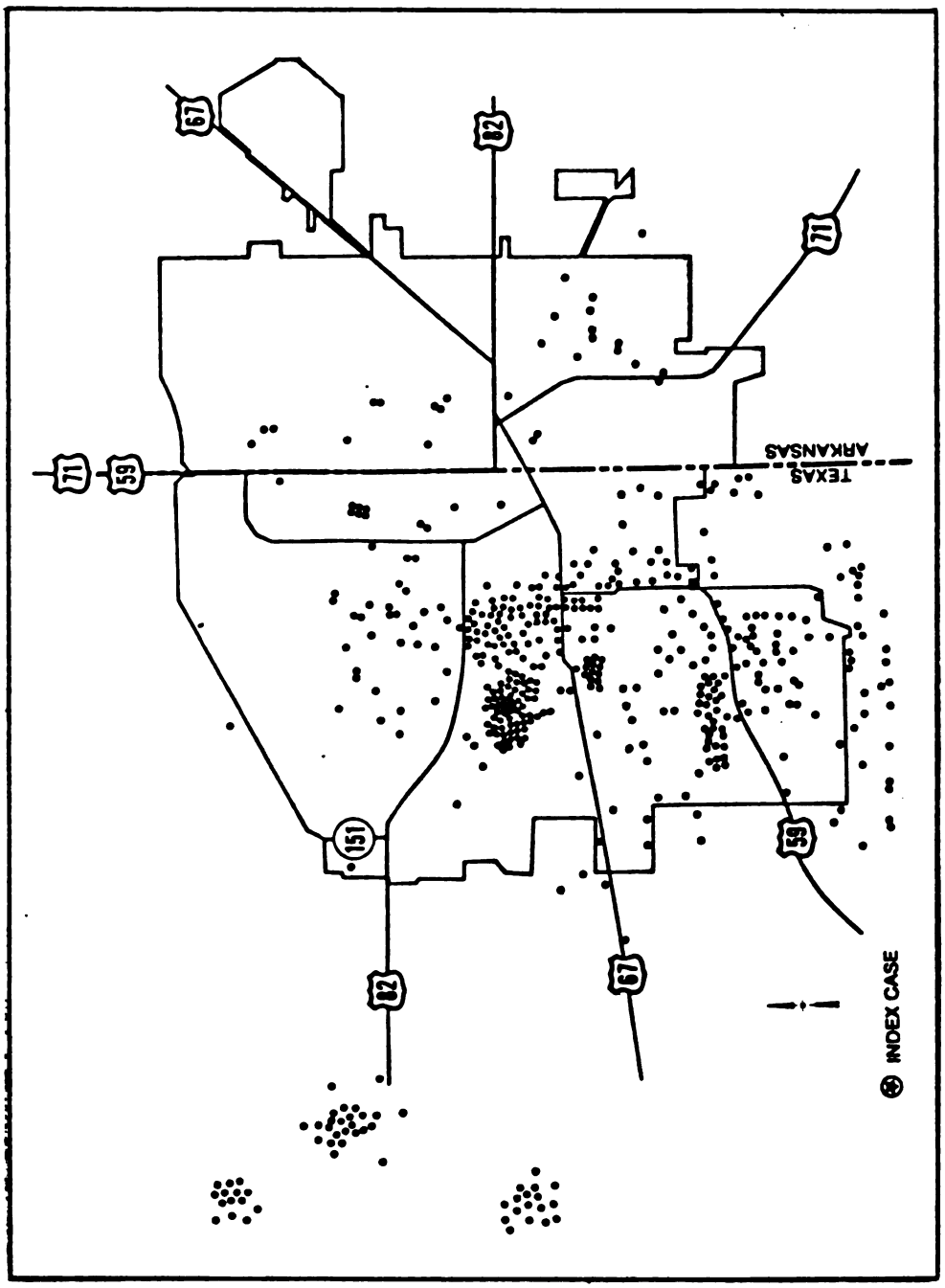
One of the most graphic examples of the efficacy of state immunization campaigns is presented in Landrigan's (1972) study of Texarkana, a city divided by the Texas-Arkansas boundary. This city is considered a single socio-economic unit, with both sides (similar in population structure) sharing most facilities except public school systems and public health departments.

A map of measles cases in Texarkana following an epidemic wave showed a significant maldistribution within the city (Figure 10). Texarkana, Texas reported 606 cases (85.7 percent) with an attack rate of 48.2 per 1,000 in children ages one to nine, whereas Texarkana, Arkansas reported only 27 cases (4.3 percent) with an



SOURCE: J. J. Witte and N. W. Axnick, "The Benefits From 10 Years of Measles Immunization in the United States," Public Health Reports, Vol. 90, No. 3 (1975), p. 207 (reprinted with permission).

Figure 9.--Annual benefits and costs of immunization against measles, United States, 1963-1972.



SOURCE: P. J. Landrigan, "Epidemic Measles in a Divided City," JAMA, Vol. 221, No. 6 (1972), p. 570. Copyright 1970, American Medical Association.

Figure 10.--Cases of measles, Texarkana, Texas - Arkansas, June 1970 to January 1971.

attack rate of 4.2 per 1,000. Landrigan attributed this geographic variation in the spread of measles to inadequate use of vaccine. He noted that Texas had no legal immunization requirements for school children and the total level of immunity in children ages one to nine was 57 percent. Arkansas, on the other hand, not only enacted a state immunization law for school children but also carried out a mass measles vaccination program in 1967 and 1968 bringing the total level of immunity for that side of the city to 95 percent. In this way, enactment of legal measures in Arkansas, in addition to a massive public campaign, was successful in preventing the spread of measles within a specific geographic area (Landrigan, 1972).

The enactment and enforcement of state laws requiring immunization for school entry is one of the most common methods of improving compliance to immunization schedules. Strict enforcement of such a law in Alaska excluded from schools all children not properly immunized by a specified date, except for those with medical and religious exemptions. This particular act resulted in the exclusion of over 7,400 children (8 percent of the total enrollment) from schools throughout the state on March 1, 1977. One month later only 51 children were still out of school. A survey of a specific elementary school after the exclusion date revealed that 92 percent of the children were adequately immunized. Since February 1977 not one case of measles has been reported in Alaska. A program of routine sampling of school immunization records is currently being

developed to ensure continuing compliance with the Alaskan law (Middaugh and Zyla, 1978).

Another successful approach to raising immunization levels has been developed in Texas. This state enacted a strong school immunization law, but provided no penalties for non-compliance. Instead of excluding children who failed to become vaccinated, pressure was placed on the school for increasing immunization levels. From 1971 to 1972 the State Health Department and the Texas Education Agency coordinated a program whereby all school districts were supplied with immunization manuals and record-keeping forms; all districts reporting low levels of immunization were visited by health department personnel. Although state officials claim no penalties exist for non-compliance, the Texas Education Agency threatens school districts reporting immunization levels below 90 percent with revokation of accreditation for failure to comply with the law (Gee and Sowell, 1975).

Reports that the entire 1973-1974 Texas school population had achieved nearly 100 percent immunization levels indicate that this law was successfully implemented (Gee and Swell, 1975). The presence of several favorable factors at the right time may have been responsible for this accomplishment. These factors include public concern, a well-written law, coordination of the public and private health care sectors, cooperation by the education and public health state agencies, and legislative funding and support for a successful immunization program (Gee and Sowell, 1975).

An additional approach to improving immunization levels utilizes a personal appeal. A study conducted in a rural Appalachian community in Kentucky attempted to determine the effects of sending a personalized letter to parents, containing information about a local immunization clinic (Wallace et al., 1973). One group of parents was selected to receive a letter and a control group of parents was selected to receive information about immunization clinics through the usual mass media approach (public television and radio announcements, pamphlets, flyers, etc.) A survey of parents who had their children immunized at the clinic revealed that 71 percent went to the clinic as a result of the letter compared to 29 percent who were immunized as a result of the mass media advertising. Twenty-four percent of those who received a letter had their children vaccinated compared to a 10.5 percent compliance rate of the control group. This Kentucky study suggests that a personal letter sent to parents can double community attendance attracted by traditional mass media methods at an immunization clinic (Wallace et al., 1973).

In Denver a comparative study was carried out to determine the effects of three different techniques for improving immunization levels in elementary schools (Vernon et al., 1976). The results of Vernon's study revealed that selective parental contact and follow-up procedures resulted in significantly greater compliance than wholesale, unselective parental contact by the school. The selective method was responsible for 67 percent of the children being immunized while only 36 percent of those involved in the

unselective method had their children immunized. The third method utilized a health education campaign in which activities such as distributing immunization pamphlets and newsletters, school health projects and classroom discussions were used. This particular method had very little impact on raising immunization levels. Only 2.4 percent of the parents reported that they had their children vaccinated as a result of the health education program. Vernon's study concluded that health education campaigns in schools are not very effective.

Yokan and D'Onofrio (1978) contend, however, that health education is vital to achieving better immunization rates. Supporters of this view believe that immunization is a long-term problem and therefore additional possibilities for the application of health education methods to immunization programs should be explored. Well thought-out plans aimed at specific target populations and proper timing are considered essential elements of a successful immunization program. Research on individual decision-making and behavior is also considered important to removing barriers to immunization. The incorporation of immunization procedures into routine health care is seen as the only viable approach on a long-term basis. Intensive immunization campaigns are often successful for a while but are then usually followed by periods of apathy. Public disinterest allows immunization levels to fall until the problem becomes serious enough for another mass campaign (Yokan and D'Onofrio, 1978).

In this regard, the recent immunization programs promoted by the McDonald's Corporation may be doing more harm than good

(McDonald's Systems, Inc., 1978). Some programs have included giving away free hamburgers and french fries to children who fulfill all their immunization requirements, hosting parties for classrooms that achieve 100 percent immunization levels, administering vaccinations from mobile units in the restaurants' parking lots, and showing immunization movies in the restaurants on Saturday afternoons. These promotions appear to be worthwhile activities; reports indicate that immunization levels have been increased in some areas by these techniques. For example, 960 children and adults were immunized in a one-day city-wide immunization clinic in Schenectady, New York after "McDonaldland" characters attended a promotional press conference and awarded free french fries to every child who received shots (McDonald's Systems, Inc., 1978). Nevertheless, the continuity of McDonald's involvement in public health concerns is uncertain. The possibility exists that once the corporation loses its interest in immunization so will the public. For this reason, a comprehensive approach is encouraged, emphasizing the use of "regular sources of care" for immunization and appealing to needs and desires that will motivate individuals to take appropriate action (Yokan and D'Onofrio, 1978).

Approaches to Immunization in Michigan

No firm statewide immunization policy has been enforced during the 1970s, even though a variety of local immunization programs in Michigan have been in effect. One particularly successful example was the 1976-1977 Immunization Enforcement Program in

Detroit. In November 1976, a status report of new school entrants revealed that 14,000 of 20,000 new entrants to public schools were either inadequately immunized or had no immunization record at all (Detroit Heatlh Department, 1978). This large unprotected school population was declared a public health hazard by the Director of Public Health. To correct the situation he initiated a two-phase enforcement program. First, letters were sent to parents of inadequately immunized new entrants warning them of exclusion from school if the requirements were not properly met. This action alone resulted in 5,000 parents presenting proof of immunization to schools. The second phase consisted of the exclusion of children whose parents failed to comply with the warnings. Exclusion notices were mailed to almost half of the new entrants, resulting in an "avalanche" of demands for immunizations and an influx of school records. The effectiveness of this program is illustrated in Table 10. After the enforcement policy, immunity levels for measles increased 13 percent, thereby reducing the proportion of susceptibles to only 3 percent. The immunity level of students completely immunized changed from 32 to 75 percent, an increase of 43 percent.

A National Immunization Initiative in the late 1970s set as one of its goals the development of a system which would assure that 100 percent of all children born in the future will have access to immunization services. The Michigan Immunization Action Program was thus formed in 1978 in order to find ways to reduce the high rates of communicable diseases that exist in Michigan (Reizen, 1978).

TABLE 10.--School Enterers 1976-66 Immune Levels Before and After a School Immunization Enforcement Policy in Detroit.

Immunization	Before	After
DTP	72%	83%
Polio	65%	80%
Measles	84%	97%
Rubella	82%	97%
Completely Immunized	32%	75%
Needing Immunization	28%	22%
Status Unknown	40%	3%

SOURCE: Russell S. Charter, "Summary of the 1976-66 Immunization Enforcement Program," Detroit Health Department, 1978.

The Michigan Department of Public Health has also increased the availability of grant support to local health departments. Michigan has 47 health departments conducting free immunization clinics. Surveys indicate that each year public health workers vaccinate one-third of the children in the state. It is believed that an increase in resources to these areas will help to increase the levels of immunization throughout the state (Coohon, 1978).

During a committee meeting of the Michigan Immunization Action Program in May of 1978 some of the problems associated with the development and organization of immunization programs were discussed. Of particular concern was the state's weak immunization law which provides no penalties for non-compliance and applies only to school enterers. To correct this the Department of Health and the Department of Education joined forces in 1978 to adopt "strong positions supporting the enforcement of school entry immunization requirements and vigorous outbreak control programs" (Reizen, 1978). Between October 1978 and September 1979 local health departments distributed more than one million doses of vaccine (30 percent above the normal amount distributed). Their goal of completing the vaccination of 700,000 school children inadequately immunized against measles by October 1979 failed to be reached. By the end of 1979, 349 of the state's 577 districts still had failed to complete the program (The State Journal, December 31, 1979). The goal now is to have students in 90 percent of the state's school districts vaccinated against measles by June 1980. If the program falls way short of its

goal, federal funding for next year's vaccination program could be cut (The State Journal, December 31, 1979).

The need for continued enforcement of the state immunization law and cooperation among state agencies is obvious. Also, better coordinator between public health and private physicians' activities is needed. One survey indicated that over 75 percent of all two year olds in the state who are vaccinated receive their initial shots from private physicians (Simonsen, 1978). Continuity of care is especially important in the immunization process and thorough records should be kept by both private and public health care providers.

Immunization programs in the state must also be equipped to deal with the problem of (1) providing adequate places to carry out vaccinations, (2) gathering support and participation from media sources, (3) maintaining commitment and interest from local health departments and (4) providing liability for injuries incurred. For any program to be successful, it must also be acceptable to the public (Simonsen, 1978). Public compliance to immunization programs, whether by legal threats or friendly persuasion, provides the key to improving immunization levels. Various immunization strategies have been tried throughout the United States and some have been very successful in lowering disease rates. Knowledge of these different control methods can be very useful, as successful components of programs can be selected out and adapted to fit the needs of other populations. The application of geographic methodologies and techniques to problems of disease control and compliance by the general

public can also be very beneficial. Suggestions for improving immunization compliance and disease control strategies are discussed below.

V. SUGGESTIONS FOR IMPROVING THE CONTROL OF MEASLES

Geographic Approaches to Disease Control

Containment of measles epidemics can be greatly improved by utilizing various geographic techniques and methodologies. In addition to the usual epidemiologic method of plotting disease incidence over time, Haggett (1976) demonstrated that processes of spatial diffusion can be analyzed by plotting cases of measles by geographic areas over a certain time period. A graph showing the passage of an epidemic wave through designated areas within a region can provide health planners with a spatial perspective of the diffusion process. The sooner infected areas are identified, the sooner control measures can be implemented to interrupt further transmission of the virus. In addition, preventive measures can be established in areas of expected contagion.

The use of planar graphs to simulate different kinds of diffusion models is another technique which can be used to control infectious diseases such as measles (Haggett, 1976). Haggett was able to determine which factors were most important to the spread and persistence of measles in a population during different stages of an epidemic using a variety of planar graphs (see Section III). The impacts of immunization programs could also be evaluated by analyzing particular phases of an epidemic wave (Haggett, 1976).

Geographic analysis of the diffusion of disease information is another technique which could be utilized by health departments and disease surveillance personnel. An analysis of six measles outbreaks in the state of Oregon from December 1974 to August 1975 revealed that the median delay from onset of the first case of measles to the report of the disease to the state was 14.5 days, with a range of 11-24 days (Francis et al., 1978). Thus, most cases were not reported until the second generation of cases had already occurred. It was also found that the median delay from the receipt of the case report by the county health department to the actual administration of vaccine was 7.5 days, with a range of 2-30 days. The total effectiveness of measles containment was assessed by the time lapse between the first case report by the county to the onset of the last case in the outbreak; this median lapse was 16.5 days, with a range from 14-57 days. Spatial analysis of the diffusion of state or county case reporting within a temporal framework could indicate which components of the surveillance system need improvement. If the time between the initial outbreak of an epidemic and the administration of vaccine to the population at risk could be reduced, unnecessary cases of morbidity and mortality could be prevented.

Spatial analysis of immunity levels can also aid in the control of measles. As this paper has shown, levels of susceptibility can be determined by mapping county immunization data. The mapping approach could be enhanced by using quantitative measures of clustering such as the join-count method of spatial

autocorrelation (Haggett, 1976), the Poisson process, Geary's contiguity ratio, or the Moran autocorrelation statistic (Taylor, 1977). In this way, clusters of large susceptible populations can alert physicians and health planners to those areas capable of creating a favorable climate for the spread of measles and other infectious diseases.

Once high-risk counties have been identified, specific plans to improve immunization levels can be formulated. Hutcheson and Barid (1974) developed a methodology for conducting accurate county immunization surveys with limited personnel and limited funds. County-specific surveys of immunity levels among two year olds were set up by: (1) determining proper county sample size from computer printouts listing birth certificates, (2) collecting information such as name, address, race and educational level of the mother from birth certificates, and (3) contacting the telephone company for correct telephone numbers and the highway department for detailed county maps. Immunization levels in each county were then determined by checking immunization records at the county health department or from telephone interviews or home visits when forms at the health department were incomplete. Using this methodology, it was determined that an entire county survey could be accomplished by two persons in three days or by one person in five days at a cost of $165. Once immunity levels were determined, unimmunized and inadequately immunized two year olds were plotted on a map of each county. This information was then used to locate clinic sites for

special immunization programs and to help make decisions concerning the location of surveillance efforts.

Ideally, a multiple-scale geographic approach should be used to delimit priority target areas. For example, the counties from a quartile distribution of immunization levels containing the highest percentages of susceptibles could be surveyed in greater depth to determine which areas within the high-risk counties were most susceptible to an epidemic. A geographical analysis of immunity levels by census tracts, townships or neighborhoods would provide valuable information to health care planners; it would tell them where immunization efforts and medical resources are needed most and it might reveal information about characteristics of persons who intentionally fail to complete immunization schedules. The issue of compliance to immunization programs is a problem that requires the interaction of both medical professionals and behavioral scientists. In this way, a geographical approach to the study of compliance behavior is suggested.

Characteristics of Non-Compliers

According to the World Health Organization, one of the major weaknesses in the national health services of most developing countries has been the inability to maintain adequate immunization programs against communicable diseases. This problem obviously pervades developed countries as well, as shown above in the poor level of adequate immunization among susceptible populations in the United States. Reasons attributed to this problem include health

personnel shortages, lack of sufficient transportation and equipment, high costs of vaccines, and the lack of integrated health care centers (Hingson et al., 1977). Even when immunizations are free, are legally required, and vaccines and personnel are adequately supplied, many people do not become immunized. Apathy and procrastination are most often cited as the reasons for such behavior but a variety of other factors also exist.

Immunization compliance in the United States is particularly low among preschoolers, non-whites, and lower socio-economic groups (Hingson et al., 1977). Poor access to health care services among these groups may be one reason for low compliance rates. Persons in lower social classes generally face not only financial barriers to care but racial barriers as well. The geographic maldistribution of physicians and health care facilities in the United States further compounds this problem (Hingson et al., 1977). Other studies suggest that the degree to which a person is socially integrated will affect his/her receptivity to immunization (Moody and Gray, 1972). Research indicates that persons of lower socio-economic status (with lower levels of income and education levels) receive less exposure to the mass media than persons of higher socio-economic status. Communication sources (that diffuse information about immunization programs) are more available to persons who are active in community affairs; this exposure may exert greater social pressure on these persons to comply with immunization programs (Hingson, 1974).

Public attitudes toward immunization also have an effect on compliance rates. During two nationwide telephone surveys in 1977 and 1978, over 4,000 parents and adults were interviewed about their attitudes toward immunization (Gunn and Scatko, 1978). Parents who wished not to have their children vaccinated for specific diseases were asked to give their reasons for such a decision. One of the major reasons given for non-acceptance was a perceived lack of necessity. Twelve percent of the parents stated this as a reason. Other reasons for not accepting vaccines included (1) a belief that an outbreak would not occur where they live, (2) doubts about the seriousness of the illness, (3) doubts that one's own child would get the disease, and (4) uncertainty about vaccine safety and efficacy. Financial, religious and personal reasons were also stated.

Most people (90 percent) interviewed believed that, in general, vaccinations were moderately or very safe. Nonetheless, 32 percent of all adults felt that some immunizations were unsafe. Blacks, especially those with lower incomes, were significantly more skeptical of vaccine safety. Only 44 percent of blacks, compared to 55 percent of whites, thought vaccinations were very safe (Gunn and Scatko, 1978). Most adults interviewed (82 percent) felt that a mass immunization program was an effective way to fight a contagious disease. When asked about state immunization laws, only 80 percent of the parents were aware of such requirements, although only one percent of the population live in states without such laws. Ninety-two percent of those parents aware of their

state laws said they would have had their children immunized even if no laws existed. This finding suggests that 80 percent of the parents might not have had their children immunized without state laws and regulations (Gunn and Scatko, 1978).

A similar survey, conducted in Ohio in 1977, attempted to determine certain "patient characteristics" associated with the failure to receive immunizations (Marks et al., unpublished). Their results showed that the immunization rate increased as the educational level of the mother increased. Paternal education was also significantly (and independently) correlated with immunization rates. When the number of siblings was compared to completion of immunization, a significant inverse association was reported, with lower rates of completion occurring in larger families. A combination of correlations further determined that, compared to a family where both parents are college graduates, a child who has at least one parent with less than a high school education or has three or more siblings, regardless of parental education, has four times the relative risk of failing to complete the immunization series (Marks et al., unpublished). This same study reported that persons living in Standard Metropolitan Statistical Areas (SMSAs) were found to be better immunized than persons living in non-SMSAs. Within SMSAs, white patients were more likely to have completed their immunization schedules than black patients. When socio-economic status was controlled for, however, the association with race failed to be significantly related.

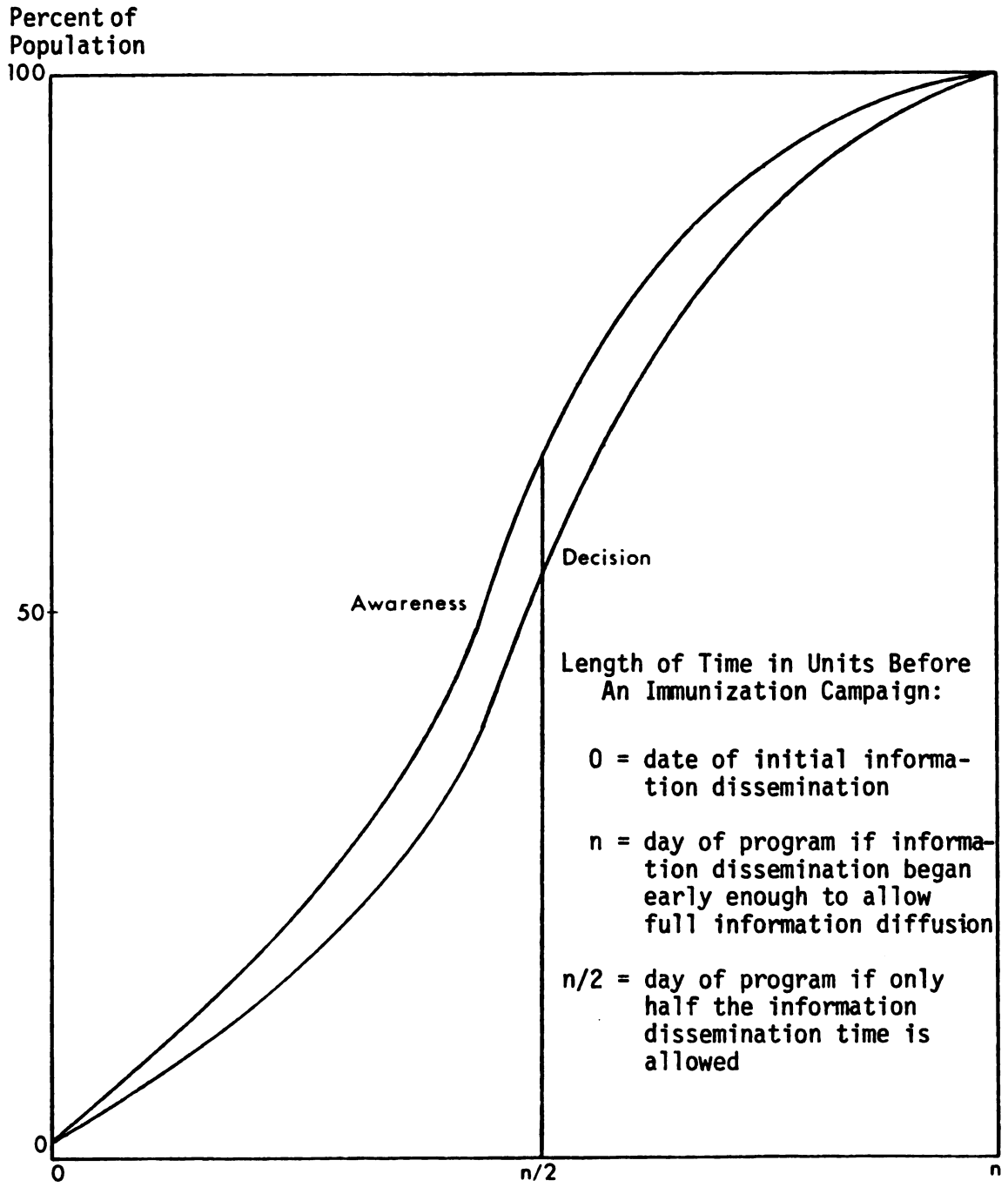
One particularly interesting aspect of the association between socio-economic status and immunization was brought out by Marks et al. (unpublished). They found that patients of low socio-economic status who went to private physicians were better immunized than patients of low socio-economic status who went to health departments. This may occur either (1) because private physicians are more effective in motivating patients to continue visits for preventive care or (2) those patients who choose to see a private physician are more motivated in health related matters to begin with and are thus more likely to continue an immunization series than persons who attend public clinics (Marks et al., unpublished).

Suggested Approaches for Improving Compliance

Several suggestions have been made above concerning methods to improve compliance. One way to improve receptivity to immunization calls for changing the health beliefs of a population. This approach is considered very difficult since health beliefs may vary between and within populations, making it hard to focus on a target population (Hingson et al., 1977). Another strategy consists of implementing legal measures, such as school immunization laws. Although successful in many situations, problems with this method stem from (1) the failure to reach certain segments of the population (such as preschoolers and immigrants) and (2) the lack of appropriate penalties for non-compliance. Fear-arousal techniques have been tried but there is some doubt concerning their effectiveness. It has been suggested that appeals to other emotions and

beliefs such as love, joy, parental affection, responsiblity, and community loyalty be investigated as an alternative method (Hingson et al., 1977).

Specific steps for persuading target populations to attend mass immunization clinics have also been proposed. The first, and most important recommendation, is to know the socio-economic characteristics of the target population (Hingson et al., 1977). Without this knowledge, a proper judgment of the applicability of different strategies is impossible. The second suggestion is to start information dissemination about a program early in order to allow time for it to reach the target population. Research on the diffusion of innovation shows that the diffusion of new information follows an S-shaped curve. A similar curve results from the diffusion of information about immunization programs (Figure 11). The acceptance of immunization as an innovation can be viewed as a three-step process: (1) making people aware of immunization availability, (2) persuading them to decide to become immunized, and (3) making immunization easily obtainable (Hingson et al., 1977). If information concerning an immunization program is not given enough time to diffuse through the population, some of those who have received the information will be unable to make a decision about becoming immunized and some may never learn about the program at all (Figure 11). Hingson (1974) suggests three weeks as the minimum amount of time to allow for dissemination of immunization information. This time period would have to be adjusted, however,



SOURCE: R. Hingson, "Obtaining Optimal Attendance at Mass Immunization Programs," Health Services Reports, Vol. 89, No. 1 (1974), p. 57.

Figure 11.--Hypothetical diffusion of information about an immunization program and decisions to receive an immunization in a target population.

to overcome social and behavioral barriers to diffusion that exist among different population groups (Gould, 1969).

Planners of immunization campaigns would also be wise to use more than one communication medium in order to assure exposure throughout the population. Public information should be delivered in an intelligent, believable, and forthright manner. Discussion of the program should be encouraged and attendance should be made as easy as possible. It is usually wise to choose immunization centers that are centrally located, have access to public transportation, and are located in familiar buildings such as shopping centers and schools. Finally, the program should be evaluated both before and during the immunization program in order to assess the impacts of the program and to allow alternative strategies to be implemented if needed (Hingson, 1974).

Another suggested strategy for improving compliance consists of identifying those people most likely <u>not</u> to become immunized (Gunn and Scatko, 1978). A mathematical model to predict vaccine acceptance among populations is currently being developed. According to Gunn and Scatko the model, based on demographics, health beliefs and respondent immunization history, should be able to correctly identify and predict about 75-80 percent of those who will not want specific immunizations.

It is further proposed that identification of non-compliant populations could be used to develop intervention strategies. Marks et al. (unpublished) found that although 98 percent of children in their study had made at least one visit to a public or private

health care provider for vaccination, over 25 percent had not completed the minimal immunization series. Thus, "If the children at high risk for failure to complete immunizations can be identified at the initial visit, then selective strategies can be developed to improve their adherance to the desired schedule" (Marks et al., unpublished). This strategy is currently being adopted by the Kent County Health Department in Michigan. Officials reported that 51 percent of children who start their immunizations at health departments fail to complete the full schedule (Ryan, 1978). To correct this situation, a computer tracking system is being established whereby parents of preschoolers who fail to follow through on their schedules within a designated time period will be contacted by the health department. Follow-up attempts will consist of telephone calls and letters and (if these first two methods fail) home visits by Public Health Nurses. It is hoped that this aggressive kind of follow-up, assisted by a computer data system, will raise the level of immunization compliance in Kent County (Hart, 1979).

Tracking systems such as the one discussed above would benefit greatly from a multiple-scale spatial analysis of non-complying areas. Immunization and attitudinal surveys carried out at a local level (census tract, township, or neighborhood block) could identify populations at risk to non-compliance. In this way, target areas could be precisely defined by geographic area as well as by socio-economic and ethnic characteristics. Intensive follow-up efforts and campaigns could then be focused on hard-core areas resistant to acceptance of regular immunization programs. A target

area approach to improving rates of immunization compliance could thus result in a more efficient and effective method of locating immunization clinics and a savings of time and money by local and state health departments.

VI. SUMMARY AND CONCLUSIONS

The control of measles is a continuing health problem in the United States which has yet to be resolved. Historically, the development of vaccines for communicable diseases such as measles greatly reduced morbidity and mortality rates throughout the country. Public health campaigns conducted at national, state and local levels provided for mass distribution of vaccines to susceptible populations. The distribution of the measles vaccine throughout the United States in the mid-1960s brought about a drastic reduction in the incidence of illness and death from measles, suggesting that eradication of the disease was possible. A significant increase in the number of measles cases reported since the late 1960s, however, demonstrated that the availability of the measles vaccine alone was insufficient to bring this infectious disease under control.

Vaccine failures, as a result of improper storage and handling methods, and the age at which vaccine was administered, contributed only a small proportion of the measles cases in the 1960s and 1970s. Instead, the overwhelming majority of measles cases occurred in unvaccinated persons. Epidemiological studies of measles epidemics in the United States revealed that the disease occurred more frequently in areas of lower socio-economic status

and in inner city areas. Attack rates were generally highest in preschoolers in urban areas, in children five to nine years old in suburban and rural areas and in black populations. Regional concentrations of measles in the United States were also evident, with the majority of cases being reported from the East North Central states.

Michigan, one of the East North Central states, was examined in this paper as an example of an area in which measles control was exceptionally poor. Epidemic outbreaks in Michigan in 1978 caused over 8,000 cases of measles, resulting in 1 death, 1 case of encephalitis, 13 cases of pneumonia and 50 hospitalizations, all of which were preventable. An epidemiologic investigation of measles in Michiagn revealed that although overreporting and lack of case verification may have exaggerated the number of actual measles cases, Michigan still ranked second in the nation (behind Maine) in rates of measles after estimates of incidence were adjusted downward. Spatial analysis of immunity levels in Michigan revealed that clusters of large susceptible populations existed in Michigan between 1976 and 1979. Counties in the highest quartile of susceptibles should be viewed as high-risk areas, capable of perpetuating epidemics and requiring the greatest improvements in communicable disease control.

Approaches to measles control in other states that have been successful in preventing epidemic outbreaks and/or raising immunization levels have included mandatory state laws, enforced school entry requirements, well-funded immunization campaigns,

personal appeals and behavioral reinforcement techniques. The lack of any of these approaches on a statewide basis in Michigan may account for its poor record of measles control. Intensified efforts during the late 1970s, including increased grant support to local health departments for immunization programs and the campaign to vaccinate all school beginners throughout the state, should reduce the size of future measles outbreaks in Michigan.

In addition, other approaches to disease control need to be considered. Two goals that should be a part of any disease control program are containment of disease transmission and prevention of disease development. The application of geographic methodologies to problems of diffusion is suggested as one way to reach the goal of containment. Spatial analytical techniques such as planar graph analysis, diffusion modelling and autocorrelation of geographic areas would greatly benefit health planners concerned with contagion surveillance and prevention. The prevention of disease outbreaks can best be attained by identifying populations that pose the greatest threat to the development of an epidemic, that is, all unimmunized persons. Persons may remain unimmunized because they have intentionally failed to comply with immunization schedules or because immunization procedures and programs are inaccessible, unavailable or unacceptable. In either case, the problem consists of a gap in the distribution of vaccine to populations at risk.

Multiple-scale geographic approaches to identification of target populations are therefore recommended. If a low level of immunity exists within an area because the majority of the

population lacks adequate access to immunization clinics, spatial analysis of the distribution of the susceptible population, transportation networks, and public transportation services could provide rational suggestions for potential immunization sites. If, on the other hand, immunity rates within a community are low because of intentional non-compliance to immunization programs, attitudinal surveys of susceptible populations could be conducted to determine which kinds of behavioral or psychological strategies would be most effective in distinct geographic areas of a city, in various ethnic groups, and in different socio-economic segments of the population. In these ways, multiple-scale spatial analysis of high-risk areas should be used as a tool to implement appropriate strategies for the control of measles and other infectious diseases.

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GEOGRAPHIC ASPECTS OF HYPERTENSION

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ABSTRACT

GEOGRAPHIC ASPECTS OF HYPERTENSION

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Essential hypertension is a highly prevalent, non-randomly distributed disease in the United States whose etiology remains unknown. Prevalence studies indicate that the risk of developing hypertension is greater in males than females, and greater in blacks than whites; furthermore, the risk increases with age. Hypertension morbidity and mortality rates are highest in the Southeastern United States and among persons with the lowest income and educational levels. A literature review shows that genetic variables, such as familial aggregation, skin color, and physiological regulatory mechanisms, and a variety of environmental variables, including lifestyle, consumption habits, stress, urbanization, altitude, water quality, and trace metals, are associated with hypertension, although there are conflicting results. Multiple-scale spatial analysis of hypertension and the use of interdisciplinary approaches to modelling are suggested as ways to improve the identification of high-risk populations and high-risk environmental variables.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

I. INTRODUCTION

Essential hypertension affects over 23 million people in the United States, yet its etiology continues to confound medical experts (National Center for Health Statistics, 1977). A wide array of etiological factors are believed to be associated with hypertension. Hypotheses involving genetic, socio-economic and environmental variables have been offered but the existence of a causal relationship between hypertension and a definitive agent has yet to be substantiated. Research indicates that the development of hypertension depends on the interplay of a number of physiological, social, cultural, psychological and environmental factors (Scotch, 1963; Stamler et al., 1967; Dawber et al., 1967). In this way, an interdisciplinary approach to its understanding appears to be the most beneficial.

The unequal distribution of hypertension among population groups at regional, national and international levels suggests that geography plays a definite role in the study of hypertension (Rose, 1962, Apostolides, 1974; Morton et al., 1975). This paper therefore examines the geographic aspects of hypertension, with an emphasis on its spatial distribution at different scales and its association with a variety of environmental variables. Compliance to hypertension regimens and follow-up programs is a major issue and was originally

to be included in this paper. The complex nature of the compliance problem became too unwieldy to be manageable in a paper of this size, however; it is therefore only mentioned as another aspect of hypertension that could benefit from a geographic approach.

This paper includes three main sections. In order to provide the proper medical background, significant clinical aspects of hypertension and its sequelae are presented first. The epidemiology of hypertension is then examined in terms of the distribution of the disease throughout various populations, by age, sex, ethnicity and geographic regions in the United States and the world. Finally, genetic and environmental etiologies of hypertension are reviewed.

II. CLINICAL SIGNIFICANCE OF HYPERTENSION

Definition

One of the major difficulties encountered when dealing with hypertension is the lack of a firm definition (Dollery, 1979). Hypertension is another word for high blood pressure and is usually defined in relation to the "normal" blood pressure values of a population. Blood pressure values among populations are skewed toward the right (higher values), however, and are therefore not normally distributed. Since there is no "natural" separation of normal and abnormal values of blood pressure, definitions of hypertension are empirical and arbitrary.

Hypertension may be defined in terms of systolic readings only, diastolic readings only, either systolic or diastolic readings or the combination of both systolic and diastolic blood pressure values. A commonly cited definition of hypertension is the one established by the World Health Organization. This definition uses the following criteria for classifying hypertension:

Definite Hypertension	$\geq$ 160/95 mm Hg
Borderline Hypertension	= 140/90 to 159/94 mm Hg
Normal Range	< 140/90 mm Hg

These criteria are among the most commonly utilized definitions in epidemiologic studies of hypertension (Smith, 1977, p. 468).

In an atttempt to further refine the definition and to act as a guide for treatment, various stages of hypertension have been delineated (Freis, 1974). These stages range from borderline hypertension, in which a patient may have occasional normal readings, to severe hypertension, in which a patient may require immediate hospitalization. The guidelines used in the evaluation of each stage of hypertension vary with individual physicians and clinics. One recommended categorization is shown in Table 1.

Since the blood pressure level is the most important single criterion for correctly diagnosing the degree of hypertension, it is particularly important to obtain a truly representative blood pressure reading. Blood pressures within individuals vary widely with different emotional states and activity levels, thereby creating major difficulties in the evaluation and classification of hypertension. Recorded variations in blood pressure during a 24-hour period have shown ranges as great as 150/74 mm Hg to 244/105 mm Hg and 110/90 mm Hg to 220/165 mm Hg in some individuals (Freis, 1974). The higher values are associated with emotional states which stimulate the sympathetic nervous system while the lowest values are associated with periods of sleep.

The apprehension felt by people visiting a doctor adds to the problem of unreliable blood pressure recordings. A reading taken at the beginning of a consultation is almost always higher than one taken near the end (Dollery, 1979). Also, the first visit to a new doctor or office makes most people nervous and anxious and usually results in a higher blood pressure reading than that which

TABLE 1.--Stages of Hypertension.

BORDERLINE:	Average blood pressure readings of 150/90 to 160/100 mm Hg with occasional normal readings and no evidence of target organ damage.
MILD:	Average of three diastolic readings between 90 and 104 mm Hg at three or more visits
MODERATE:	Average of 105 to 114 mm Hg diastolic blood pressure over three or more visits.
MODERATELY SEVERE:	Average diastolic blood pressure in the range of 115 to 129 mm Hg.
SEVERE	Diastolic blood pressure of 130 mm Hg or higher.

SOURCE: E. D. Freis, "The Clinical Spectrum of Essential Hypertension," Archives of Internal Medicine, Vol. 113, No. 6 (1974), pp. 982-987.

would occur at other times. Systolic blood pressures have been found to drop ten mm Hg from the first to the second office visit and about four mm Hg from the second to the third visit (Dollery, 1979). In sum, a single "casual" blood pressure reading (that is, a reading taken on a first visit without any special preparation) is often unrepresentative of a patient's actual blood pressure. Unfortunately, this single reading seems to be the most common method of blood pressure measurement by physicians and in epidemiologic surveys. It is recommended that, whenever possible, multiple blood pressure readings should be used to diagnose hypertension, either over the course of several clinic visits or allowing for rest periods between measurements during a single visit (Dollery, 1979).

Recently, blood pressure measurement training programs have been somewhat successful in teaching people how to take their blood pressure in their own homes, thereby reducing the anxiety induced by a foreign environment and increasing the individual's knowledge and awareness of hypertension. It has even been proposed that the home blood pressure reading approach be used in epidemiologic studies in order to assure more accurate and more standardized blood pressure measurements (Kesteloot and Joossens, 1978).

Clinical Mechanisms

Systemic arterial pressure is regulated by four main control systems--the arterial baroreflex, the regulation of body fluid volume, the renin-angiotensin system and vascular autoregulation.

These mechanisms maintain the blood pressure level needed to keep the brain and eye functioning and to allow pressure filtration in kidneys and perfusion of the coronary arteries. They are also responsible for preventing the blood pressure from rising too high, which results in vascular damage. Each of these mechanisms aids in blood pressure regulation in normotensive and in hypertensive individuals. It is still uncertain, however, to what extent each mechanism influences the pathogenesis of hypertension (Dollery, 1979).

Symptomatology

Hypertension is often referred to as "the silent killer" because its victims usually show no symptoms. The elevated level of blood pressure itself is often the only notable clinical finding. Headache, dyspnea, giddiness, and blurred vision are sometimes experienced by persons with mild to moderate hypertension, however, none of these symptoms are directly caused by hypertension (Dollery, 1979). Some patients not in the accelerated stage of hypertension exhibit retinal changes. These include a narrowing of the arterioles and thickening of the vessel wall as a result of muscle hypertrophy and fibrous replacement. Such features are usually found in normotensive elderly persons and thus are not exclusively characteristic of hypertension (Dollery, 1979).

Severe hypertension usually results in complications of the cardiovascular system and the brain. This may include signs of left ventricular failure, basal crepitations in the lungs, a third heart

sound, pulsus alternons, or congestive heart failure with a raised jugular venous pressure and peripheral edema (Dollery, 1979).

Sequelae

Hypertension in itself is not an important clinical disease. It is, however, "the most important single factor that enables a physician to make a prediction about the future risk of vascular disease, and . . . it is a risk that can be controlled by lowering the blood pressure" (Dollery, 1979, p. 1200).

Several studies have been conducted to calculate risks associated with certain levels of blood pressure. Not surprisingly, life insurance companies were among the first to recognize that factors such as high blood pressure, overweight and proteinuria were associated with higher mortality rates. From 1935 through 1954, 26 life insurance companies collaborated on an analytical study of mortality rates among nearly four million policy holders. The study evaluated risk factors to predict the development of illness or death based on 102,000 deaths among the insured population during this 20-year period (Society of Actuaries, 1959).

A statistically significant higher risk of premature death was found in men with hypertension. The risk of death was 144 percent higher in men with systolic pressure between 158 and 167 mm Hg compared to the risk of death of normotensives. For women with systolic pressure between 158 and 167 mm Hg the increased risk of death was 130 percent. Even those with only mildly elevated blood pressures had increased risks of death. Diastolic pressures between

88 and 92 mm Hg resulted in a 50 percent greater risk of death in men and a 22 percent greater risk of death in women (Society of Actuaries, 1959).

Most deaths among persons with hypertension are caused by damage to blood vessels in vital organs, resulting in myocardial infarction, stroke, peripheral vascular disease and renal failure. The only causes of death directly related to the blood pressure level at the time of death are accelerated hypertension, cerebral hemorrhage, heart failure and dissecting aneurysms. Myocardial infarction is the most important of these as it is responsible for more than half the deaths in hypertensive individuals (Dollery, 1979).

In order to examine the association between hypertension and cardiovascular disease, over 5,000 subjects in Framingham, Massachusetts were followed prospectively for periods up to 20 years. Eight biennial exams were conducted between 1950 and 1964; some subjects received further examinations after 1964 (Singer and Levinson, 1976). In these landmark Framingham studies blood pressure was recognized as one of many cardiovascular risk factors. In importance, it was determined to be "the most potent prevalent contributor to cardiovascular morbidity and mortality" (Kannel, 1975, p. 1).

Based on the W.H.O. definition of hypertension, mortality ratios and excess death rates were calculated for Framingham males and females 35 to 64 years old (Table 2). Excess mortality was consistently observed over the 12-16 year follow-up period in hypertensive groups, ranging from 130 percent to 188 percent for borderline hypertensives and from 205 percent to 310 percent for

TABLE 2.--Observed Data and Long-Range Experience by Entry Age and Hypertension Status 12-16 Years Later: The Framingham Studies.

Entry Age (years)	Hypertension Status	Number of Entrants	Number of Deaths[a]	Mortality Ratio[b]	Excess Death Rate[c]
MALES:					
35-44	Normal	1,490	90	--	--
	Borderline	833	65	132%	1.4
	Definite	322	49	265%	7.3
	All	2,645	204	130%	1.3
45-54	Normal	1,062	124	--	--
	Borderline	734	148	182%	7.2
	Definite	419	130	300%	17.0
	All	2,215	402	161%	5.4
55-64	Normal	643	145	--	--
	Borderline	477	146	143%	7.7
	Definite	316	161	275%	31.0
	All	1,436	452	147%	8.5
FEMALES:					
35-44	Normal	2,454	104	--	--
	Borderline	647	45	165%	2.0
	Definite	204	21	250%	4.6
	All	3,305	170	123%	0.7
45-54	Normal	1,243	94	--	--
	Borderline	931	91	130%	1.7
	Definite	566	84	205%	5.8
	All	2,740	269	132%	1.8
55-64	Normal	520	47	--	--
	Borderline	664	108	188%	5.9
	Definite	605	155	310%	14.0
	All	1,789	310	200%	6.8

SOURCE: R. B. Singer and L. Levinson, Medical Risks: Patterns of Mortality and Survival (Lexington, Mass.: D. C. Heath and Co., 1976), pp. 3-78.

[a]Between first and ninth exam.

[b]Based on expected death rates of male and female normotensives.

[c]Per 1,000 persons

definite hypertensives. Excess deaths per 1,000 persons per year ranged from 1.4 to 7.7 among borderline subjects and from 4.6 to 31.0 among hypertensive subjects (Singer and Levinson, 1976). These figures are notably higher than those reported in the Build and Blood Pressure Study (Society of Actuaries, 1959) but they are more representative of the general population since the insured group represented a selected group of relatively healthy persons.

Further examinations of the Framingham data revealed that: (1) 65 percent of all mortality in hypertensives was from cardiovascular disease, (2) mortality rates in hypertensives were twice as high as in normotensives, and (3) cardiovascular mortality was three times higher in hypertensives (all ages, both sexes) than normotensives. Risk varied widely among hypertensive subjects depending on factors such as elevation of blood pressure, presence of left ventricular hypertrophy, serum cholesterol values, carbohydrate tolerance, cigarette smoking and heart size on x-ray. Not only were cardiovascular attacks more frequent in hypertensives but they were also more likely to be fatal (Kannel, 1975).

Another investigation in Framingham, Massachusetts was concerned with the relationship between hypertension and congestive heart failure (Kannel et al., 1972). A prospective study of 5,192 men and women aged 30-62, followed for 16 years, revealed that hypertension preceded congestive heart failure in 75 percent of the cases. The risk of developing congestive heart failure was six times greater in hypertensives than in normal subjects (Kannel et al., 1972). Hypertension was also found to be the most common and potent

precursor of stroke (Kannel et al., 1970). In general, hypertensives had a risk factor four times greater than normal subjects for developing stroke. Among 40-49 year olds, however, the risk of stroke was ten times higher in those with diastolic pressure greater than 104 mm Hg compared to those with a diastolic pressure less than 85 mm Hg (Kannel et al., 1970).

Treatment

Since hypertension is a chronic condition, treatment is usually long term. Antihypertensive medication consists of four main groups of drugs: diuretics, beta receptor-blocking drugs, vasodilators and centrally acting sympathetic inhibitors. Unpleasant side effects occur with many of the drugs prescribed and it often takes several months or years to find the level and/or combination of drugs best suited to an individual. Once drug treatment has begun, it can rarely be stopped. Blood pressure may return to pre-treatment levels after drug treatment is terminated. It usually starts to rise slowly over a few weeks or months (Dollery, 1979).

The effectiveness of hypertension treatment was demonstrated in a series of studies conducted by the Veterans Administration. Antihypertensive therapy was found to be very beneficial among hypertensives with diastolic pressures ranging between 115 and 129 mm Hg. Patients receiving active treatment averaged reductions of 43 mm Hg systolic pressure and 29.7 mm Hg diastolic pressure after two years while those receiving placebos showed no significant

changes in blood pressure. Of 143 patients, complications occurred in 27 of those in the placebo-treated group and in 2 of those receiving antihypertensive drugs, a difference significant at $p < .001$ (Veterans Administration Cooperative Study Group, 1967).

Further studies revealed that the higher the level of blood pressure, the greater the benefit of therapy. Thus, although the effectiveness of treatment was clearly demonstrated for systolic blood pressures greater than 164 mm Hg and for diastolic pressures greater than 104 mm Hg, its effectiveness is less clear cut below these levels. Antihypertensive treatment is most effective in preventing hypertension complications such as hypertension neuroretinopathy. Treatment is least effective in preventing atherosclerotic complications which are most common in mild hypertensives (Veterans Administration Cooperative Study Group, 1970).

Current recommendations concerning the treatment of hypertension are based on the blood pressure levels shown in Table 3. Individuals with mild hypertension should be carefully monitored every six to nine months but drug therapy is usually not suggested. Treatment, such as the use of diuretics and diet modification, should be individualized at this stage (U.S. DHEW, 1977).

All persons with diastolic pressures greater than 105 mm Hg should be treated. Group Two and Group Three hypertensives usually receive one or more of the drugs listed, according to the "stepped care approach." This approach consists of initiating therapy with a small dose of one drug, increasing the dose of that drug as needed, adding other drugs if necessary, and stepping up

TABLE 3.--Treatment Protocol for Hypertension.

Stage of Hypertension	Diastolic Pressure	Recommended Therapy
Group 1	(90-104)	Diuretics, weight loss, salt restriction, possibly drug therapy.
Group 2	(105-129)	Diuretics, Rauwolfia Compounds, Methyldopa, Propanolol, Hydralazine, Guanethidine, Clonidine, Prazosin
Group 3	(130 & up)	Diuretics, Rauwolfia Compounds, Hydralazine

SOURCE: United States Department of Health, Education and Welfare, Detection, Evaluation and Treatment of High Blood Pressure, National Institutes of Health, DHEW Publication No. (NIH) 77-1088.

as needed to reach the patient's goal. The official goal of antihypertensive therapy is to achieve and maintain a diastolic pressure less than 90 mm Hg and this reportedly can be accomplished in 80-85 percent of hypertensives regardless of the initial severity of the blood pressure level (U.S. DHEW, 1977).

It is often emphasized that control of hypertension is a lifelong endeavor and demands a regimen to which many patients cannot adhere. Failure to comply with the physician's advice is a most common cause of treatment failure (Dollery, 1979). It is hoped that, by careful patient monitoring, use of the stepped care approach to minimize side effects, and more rigorous follow-up techniques, the management of hypertension will be more successful.

III. EPIDEMIOLOGY OF HYPERTENSION

Prevalence in the United States

Numerous epidemiological studies have been conducted to determine the prevalence of hypertension within defined populations (Stamler et al., 1976; Hypertension Detection and Follow-Up Program Cooperative Group, 1977; National Center for Health Statistics, 1977). These studies provide a useful measure of the distribution of the disease throughout populations according to age, sex, race and other parameters. The problem with most of the epidemiological studies carried out to date is that they fail to standardize the data and that data utilized are not directly comparable. Studies such as those mentioned above vary according to hypertension criteria, methods of blood pressure measurement, type of setting in which blood pressure is taken (clinic, home, school) and population composition. All of these factors may influence the results of an investigation.

Several massive blood pressure screening programs were carried out in the United States during the 1970s. One of these, the Health and Nutrition Examination Survey of 1971-74, examined 17,854 persons nationwide between the ages of 6 and 74 years from a national probability sample (National Center for Health Statistics, 1977). A single blood pressure reading was taken for each person; the W.H.O. criteria for hypertension were used.

The results from this survey suggested that 23.2 million adults (18.1 percent of 18-74 year olds) have definite hypertension. An additional 24.8 million (16.2 percent of the population 12-74 years old) are borderline hypertensives. Prevalence rates are slightly higher among men (19.2 percent) than women (17.1 percent) and much higher among blacks (30.5 percent) than whites (16.8 percent). Table 4 presents the age, sex, and race breakdowns of definite hypertension with standard errors of rates and age-adjusted values. In this table, the age-adjusted values are much more meaningful than the unadjusted rates because of the different age composition of the black and white population.

Prevalence of hypertension increases with age among all races and for both sexes, with rates ranging from 0.8 percent among 12-17 year olds to 40.7 percent among 65-74 year olds. Before age 15, blood pressures are similar between the sexes, but pressures for boys exceed those of girls from 15 years until age 54, when the trend is somewhat reversed. Between the ages of 18 and 34 hypertension is twice as prevalent in men than women but between the ages of 65 and 74, 40 percent of women and 37 percent of men are hypertensive (National Center for Health Statistics, 1977). Of particular interest in these data is that 25 percent of those with definite hypertension have substantially elevated diastolic pressure of 105 mm Hg or more. Once again, the prevalence rates are higher among males (28.1 percent) than females (24.9 percent) and among blacks (38.0 percent) than whites (24.0 percent) (National Center for Health Statistics, 1977).

TABLE 4.--Rate and Number of Persons 12-74 Years with Definite Hypertension, by Race, Sex, and Age with Standard Errors of Rate and Age-Adjusted Values: United States, 1971-1974.

Sex and age	All races[1]			White			Negro		
	Rate per 100 persons	Standard error of rate	Population in thousands	Rate per 100 persons	Standard error of rate	Population in thousands	Rate per 100 persons	Standard error of rate	Population in thousands
Both sexes									
12-17 years	0.8	0.20	206	0.7	0.22	145	1.2	0.72	40
18-74 years	18.1	0.58	23,171	17.0	0.57	19,359	28.2	1.75	3,672
18-24 years	3.1	0.58	738	3.1	0.65	632	3.7	1.06	106
25-34 years	6.6	0.67	1,777	5.8	0.65	1,373	13.7	2.86	401
35-44 years	15.5	1.12	3,492	13.6	1.09	2,738	32.0	3.85	696
45-54 years	24.2	1.64	5,702	22.2	1.59	4,710	44.0	6.31	875
55-64 years	33.2	1.66	6,257	31.4	1.59	5,354	52.6	5.24	865
65-74 years	40.7	1.60	5,205	39.3	1.72	4,551	55.1	3.87	628
Males									
12-17 years	1.1	0.37	140	1.0	0.39	115	0.2	0.17	3
18-74 years	19.2	0.77	11,656	18.5	0.84	10,000	27.8	2.33	1,595
18-24 years	4.8	1.10	544	4.9	1.29	485	4.6	1.77	59
25-34 years	9.1	1.34	1,159	8.2	1.28	912	17.7	5.98	244
35-44 years	18.9	1.92	2,043	17.3	1.97	1,706	38.2	6.55	313
45-54 years	26.8	2.12	3,022	25.8	2.06	2,611	36.8	7.95	401
55-64 years	32.3	2.18	2,875	31.1	2.14	2,529	49.9	7.86	335
65-74 years	36.6	1.74	2,014	35.3	1.85	1,757	50.1	4.28	243
Females									
12-17 years	0.5	0.24	67	0.3	0.16	29	2.2	1.44	37
18-74 years	17.1	0.76	11,515	15.7	0.72	9,359	28.6	2.28	2,077
18-24 years	1.6	0.31	194	1.4	0.30	147	2.9	1.06	47
25-34 years	4.4	0.51	618	3.7	0.57	461	10.2	1.95	157
35-44 years	12.3	1.01	1,449	10.1	0.94	1,033	28.3	4.71	383
45-54 years	21.9	1.91	2,680	18.9	1.86	2,099	50.9	7.69	575
55-64 years	34.0	2.08	3,382	31.7	2.02	2,826	54.5	7.11	530
65-74 years	43.9	2.03	3,191	42.3	2.26	2,795	58.8	4.73	385
Age-adjusted values:									
Both sexes, 18-74 years	-	...	...	16.8	...	...	30.5	...	...
Males, 18-74 years	-	...	...	18.3	...	...	30.1	...	...
Females, 18-74 years	-	...	...	15.5	...	...	31.2	...	...

SOURCE: National Center for Health Statistics, Vital and Health Statistics, Series 11/No. 203, Blood Pressure Levels of Persons 6-74 Years (U.S., 1971-1974), U.S. DHEW, Public Health Service, Washington, 1977.

[1] Includes all other races.

In 1973-74 the Hypertension Detection and Follow-Up Program attempted to identify the distribution of hypertensives in 14 different communities in the United States. The communities screened, which ranged from New York to Los Angeles and from Atlanta to Minneapolis, provided a total screening sample of 441,846 persons from 30 to 69 years old. The criterion used for defining hypertension in this study was a diastolic pressure reading of 95 mm Hg or more (Hypertension Detection and Follow-Up Program Cooperative Group, 1977). The findings of this group were similar to the Health and Nutrition Examination survey reported above. In general, blacks had higher mean blood pressures than whites and men had higher blood pressures than women. Prevalence rates ranged from two to four times higher in blacks at various ages, with the greatest difference in the younger age groups. Rates of severe hypertension (defined as a diastolic blood pressure of 115 mm Hg or more) were about six times higher in blacks than whites (Hypertension Detection and Follow-up Program Cooperative Group, 1977).

Among all hypertensives, 25 percent were newly detected, 21 percent had been previously detected but were not currently being treated, 16 percent were being treated but their blood pressure was not under control, and 38 percent were on treatment and reported a normal blood pressure. As Table 5 shows, hypertension was more often previously detected in women than in men and a higher proportion of white women had their blood pressure under control than any other sex-race group (Hypertension Detection and Follow-Up Program Cooperative Group, 1977).

TABLE 5.--Status of Actual Hypertensives: Hypertension Detection and Follow-up Program, 1973-74.

	White		Black		Total
	Male	Female	Male	Female	
Newly Detected	36%	17%	36%	17%	25%
Previously Detected, Currently Untreated	23%	18%	24%	22%	21%
Currently Treated, Uncontrolled (DBP 95 mm Hg)*	23%	13%	24%	21%	16%
Currently Treated, Controlled (DBP 95 mm Hg)	28%	52%	22%	40%	38%

SOURCE: Hypertension Detection and follow-Up Program Cooperative Group, "Blood Pressure Studies in 14 Communities," JAMA, Vol. 237, No. 22 (1977), p. 2388.

*DBP = Diastolic Blood Pressure

During this same time period (1973-74), Community Hypertension Evaluation Clinics were established at 1,171 sites in 42 states; over one million people were screened for hypertension between 1973 and 1975 (Stamler et al., 1976). One blood pressure reading was recorded and the criteria for defining hypertension was a diastolic pressure of 90 mm Hg or more or a systolic reading of 180 mm Hg or more.

Prevalence ratios were calculated for different age-sex-race groups at various levels of blood pressure. For those with diastolic pressures of 90 mm Hg and above, the black-white prevalence ratio among men 30-39 years old was 1.43. That is, hypertension was 43 percent more prevalent among black males than white males. For women the black-white prevalence ratio was 2.05. The race differences were even more dramatic at diastolic pressure levels of 110 mm Hg or more. The prevalence ratios at this level were 3.06 for males and 3.95 for females (Table 6).

As stated above, various measurements of hypertension have been used to determine prevalence rates among population groups. Although the identical prevalence rates are not reported among different epidemiological surveys, the general pattern of the distribution of hypertension within a population consistently appears. From these prevalence estimates it has therefore been determined that the risk of developing hypertension is greater in males than in females and in blacks than in whites; furthermore, the risk increases with age in all ethnic groups.

TABLE 6.--Black-White Prevalence Ratios of Persons 30-39 Years Old.

	Diastolic Blood Pressure		
	90 mm Hg	95 mm Hg	110 mm Hg
Male	1.43	1.77	3.06
Female	2.05	2.58	3.95

SOURCE: J. Stamler et al., "Hypertension Screening of 1 Million Americans," JAMA, Vol. 235, No. 21 (1976).

Spatial Aspects of Morbidity and Mortality

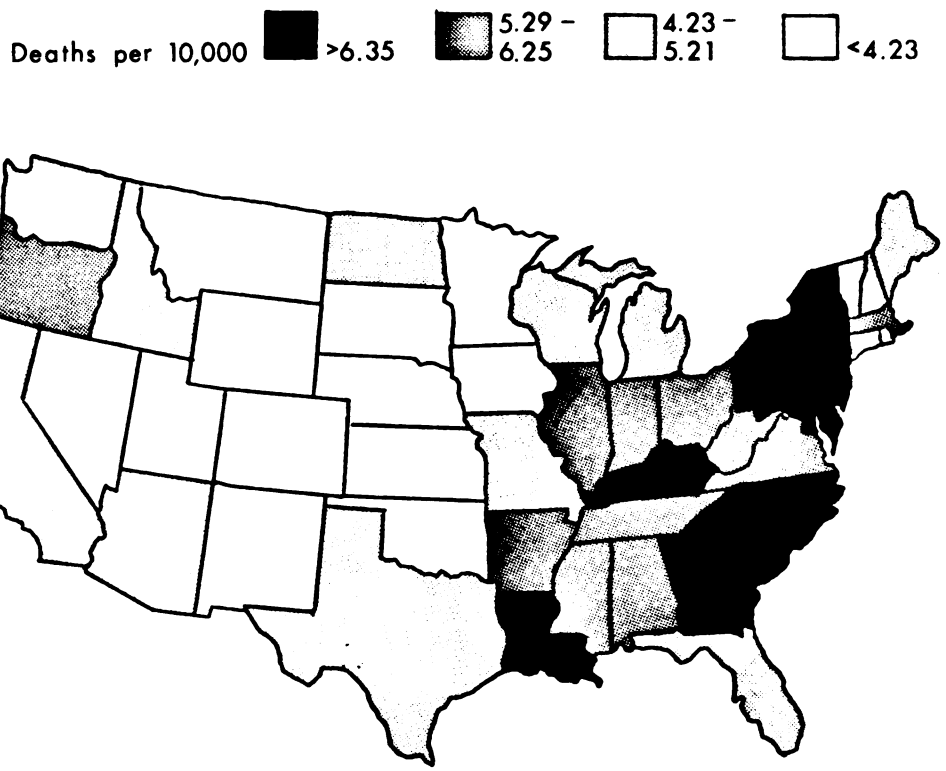
The risks of developing heart disease and cardiovascular disease from hypertension have been well established (Kannel, 1975). The high prevalence of hypertension throughout the United States has also been discussed. Although it affects large numbers of individuals, hypertension is clearly more common and more serious among particular age, sex and ethnic groups. Hypertension shows distinct concentrations in particular geographic areas as well (Rose, 1962; Morton et al., 1975).

An examination of the spatial aspects of hypertension morbidity and mortality is important for identification of high-risk areas. Health planners may use geographic data to target scarce resources into areas with the greatest need. Furthermore, identification of areas with high and low prevalence rates may provide clues to possible disease etiologies. Put simply,

> if hypertension is common in all areas of the world, we must look for some cause common to all mankind and if hypertension is common in one area and rare in another we must look for some cause present in one area and absent in the other (Schroeder, 1961, p. 81).

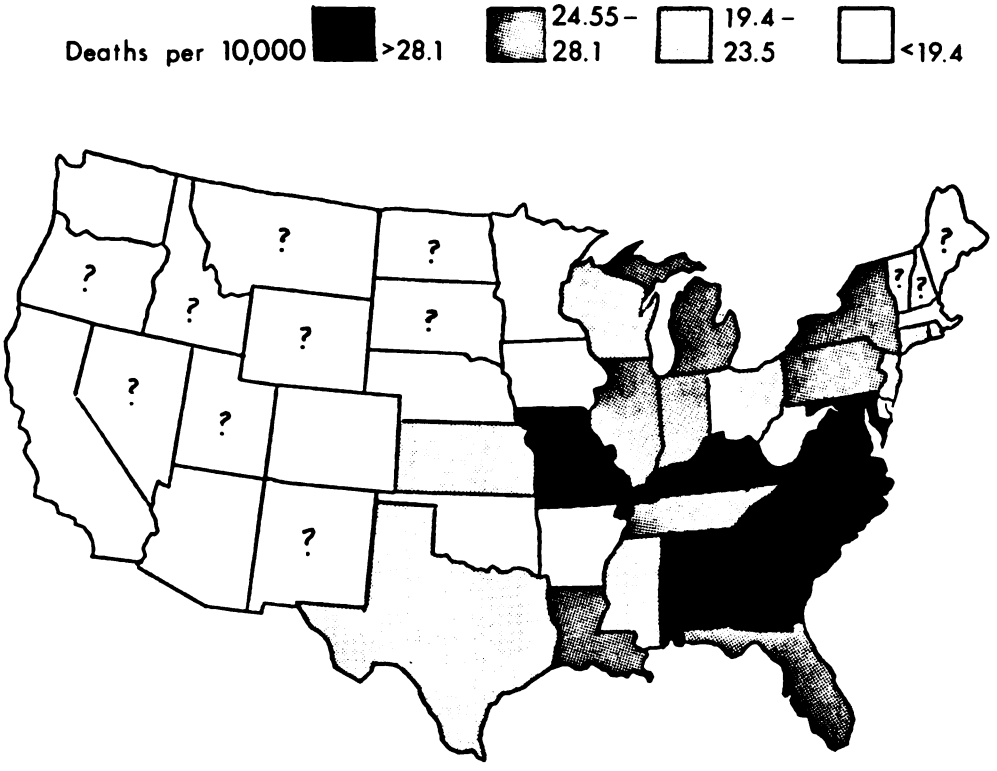
Regional patterns of hypertension morbidity and mortality are described below; explanations for these patterns are discussed separately in Section IV.

Patterns of deaths from hypertension for whites and non-whites between 1949 and 1951 are shown in Figure 1 and Figure 2 (Rose, 1962). Each state was ranked according to the number of deaths attributable to hypertension and then divided into quartiles. Males and females showed no significant regional differences in



SOURCE: G. Rose, "The Distribution of Mortality from Hypertension Within the United States," Journal of Chronic Diseases, Vol. 15 (1962), p. 1018.

Figure 1.--Age-adjusted death rates for hypertension, designated by quartiles, for the white population of the United States, both sexes, ages 40-64, 1949-1951.



SOURCE: G. Rose, "The Distribution of Mortality from Hypertension Within the United States," Journal of Chronic Diseases, Vol. 15 (1962), p. 1021.

Figure 2.--Age-adjusted death rates for hypertension designated by quartiles, for the non-white population of the United States, both sexes, ages 40-64, 1949-1951 (excluding states with rates based on fewer than twenty deaths).

mortality rates; therefore their rates were combined. All rates were age-adjusted to the 1950 population by race.

For the white population, the highest mortality rates were concentrated in a belt extending from Louisiana to New York. The lowest mortality rates were located in the Great Plains and Rocky Mountain states. South Dakota reported the lowest mortality rate (3.2 per 10,000) and Maryland reported the highest rate (9.5 per 10,000).

A similar regional pattern existed for the non-white population except that the rates and magnitude of the variation were much higher. For example, Arizona reported a mortality rate of 7.4 per 10,000 compared to 44.5 per 10,000 reported in South Carolina. The lack of data for non-whites in many of the Western states, however, made further analysis for this population impossible (Rose, 1962).

Mortality rates for hypertensive heart disease showed similar patterns among the 1960 population (Morton et al., 1975). Peak mortality rates were reported in the Southeastern states and Hawaii while the lowest rates occurred in the Great Plains, Southwest and Rocky Mountain regions and Alaska (Table 7). The 1959-61 mean mortality rates for hypertension and hypertensive heart disease also showed that the increased risk of death from hypertension in the Southeast was greater for blacks than for whites. The peak hypertension mortality rate for white females occurred in the mid-Atlantic states of New Jersey, New York and Pennsylvania.

The general pattern for morbidity from hypertensive heart disease was also consistent for deaths from cerebrovascular

TABLE 7.--States with Highest and Lowest Mortality Rates per 100,000 for Hypertensive Heart Disease, 1960.

State	Rate per 100,000*
11 HIGHEST:	
South Carolina	63.9
Hawaii	58.3
District of Columbia	58.2
Maryland	55.5
Alabama	49.6
North Carolina	48.4
Louisiana	45.7
Delaware	45.3
Mississippi	43.4
Georgia	42.0
Virginia	41.6
United States	28.2
11 LOWEST:	
Arizona	17.8
Wyoming	17.7
Idaho	17.5
Nebraska	17.2
Montana	16.8
Iowa	16.5
Colorado	15.2
New Mexico	14.8
North Dakota	14.6
South Dakota	12.3
Alaska	10.8

SOURCE: W. E. Morton, et al., "Distribution of Hypertension and Renal Disease in Oregon," Public Health Reports, Vol. 90, No. 1 (1975), p. 35.

*All rates are age-adjusted.

accidents (stroke), often associated with hypertension (Borhani, 1965). The highest mortality rates for 1960 occurred in the South Central and South Atlantic states while the lowest occurred in the Southwest and Mountain states. For example, among white males, age-adjusted death rates ranged from 34.3 per 100,000 in Wyoming to 90.3 per 100,000 in South Carolina.

Borhani (1965) attempted further analysis of this geographic clustering by using the Geary contiguity ratio. This ratio represents the degree of difference from a totally random distribution. In other words, it is a measure of the degree of clustering. A perfectly random distribution has a contiguity ratio of 1.0. The values of the contiguity ratio for males and females in 1950 and 1960 differed from unity and that clustering was more pronounced among males than females (Table 8). These differences were all statistically significant at $p < 0.01$.

This clustering pattern observed in the Southeastern United States has since become known as the "stroke belt" (Hames, 1974, p. 120). When death rates for stroke in Savannah, Georgia, for example, were compared to those of the United States as a whole, rates in Savannah were 1.5 to three times higher (Table 9).

In another investigation of deaths from stroke, death certificates of veterans from Georgia and from five selected Western states were examined. Of the death certificates that reported stroke as the underlying cause, 26.3 percent of the death certificates from Georgia had a record of hypertension while only 9.1 percent of those from the five Western states contained an

TABLE 8.--Contiguity Ratio for Age-Adjusted Death Rates from Cerebrovascular Diseases, by Sex for Coterminous United States, White Population, 1949-51 and 1959-61.

Year	Sex	Value of Contiguity Ratio
1950	Male	0.31
	Female	0.55
1960	Male	0.33
	Female	0.64

SOURCE: N. Borhani, "Changes and Geographic Distribution of Mortality from Cerebrovascular Disease," American Journal of Public Health, Vol. 55, No. 5 (1965), p. 677.

TABLE 9.--Death Rates per 100,000 Persons for Stroke in Savannah, Georgia and the United States, 1959-61.

Race and Sex	Savannah	United States
While male	206.1	114.5
White female	130.2	89.0
Black male	545.5	266.0
Black female	886.5	270.0

SOURCE: C. G. Hames, "Natural History of Essential Hypertension in Evans County, Georgia," Postgraduate Medicine, Vol. 56, No. 6 (1974), p. 121.

entry of hypertension. Furthermore, 85 percent of the deaths in Georgia in which stroke was named as the cause were natives of Southern states (Acheson et al., 1973).

The Health and Nutrition Examination Survey of 1971-74 compared blood pressure levels of four main regions in the United States--Northeast, Midwest, South and West (National Center for Health Statistics, 1977). For persons 7-74 years old, average age-adjusted systolic blood pressures in the South were significantly higher than those in the Northeast (by 3.3 mm Hg) and in the West (by 4.3 mm Hg) and were slightly higher than those in the Midwest (by 2.3 mm Hg). Mean diastolic blood pressures, however, were similar in all four regions.

In addition to regional patterns such as those described above, hypertension is more prevalent among persons with certain levels of income and education. In general, mean blood pressure levels are inversely related to both family income and educational levels (National Center for Health Statistics, 1977). Examinations of rural residents in north central Mississippi showed that those living at the most extreme level of poverty had the most severe form of hypertension (Pollner and Parrish, 1976). Persons with the least education also show 47-70 percent more hypertension than those with the most education (Dyer et al., 1976). Standardization of age, weight and education distributions results in lower adjusted hypertension prevalence rates in male and female blacks, but even when these factors were controlled, hypertension rates in blacks (approximately 33 percent) remained almost twice as high

as in whites (approximately 18 percent) (Hypertension Detection and Follow-Up Program Cooperative Group, 1977).

Urban-rural differences in hypertension prevalence have also been observed. Although most studies have shown hypertension to be more prevalent in urban areas, findings have not been consistent. In fact, several studies have reported higher prevalence rates in rural areas (Tyroler, 1977; Eckenfels et al., 1977; National Center for Health Statistics, 1977). Blacks in rural settings in Jamaica and Mississippi have shown higher mean blood pressures and higher prevalence rates of hypertension than their socio-economically comparable peers in urban places (Tyroler, 1977). In Holmes County, Mississippi, definite hypertension was recorded in 43.5 percent of black males and 39.5 percent of black females and it is considered an endemic chronic disease of this rural community (Eckenfels et al., 1977). Consistent with these findings, the Health and Nutrition Examination Survey found systolic blood pressures of those 7-74 years old to be inversely related to population density (National Center for Health Statistics, 1977).

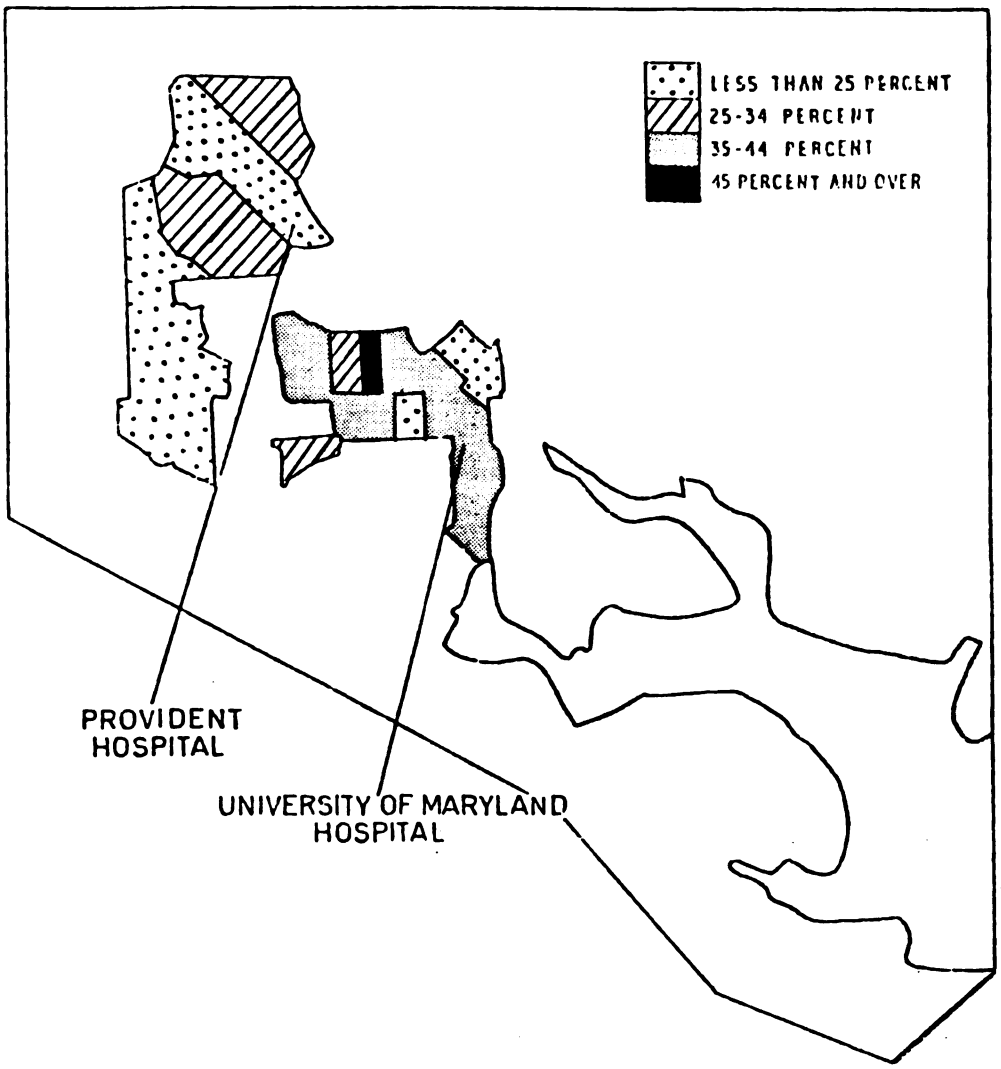
As indicated previously, however, the majority of epidemiologic studies have reported higher rates of hypertension in urban areas. A prevalence survey of black residents in the city of Baltimore, for example, suggests that "hypertension is a particular problem of metropolitan areas" (Apostolides, 1974, p. 105). Age- and sex-adjusted prevalence rates in Baltimore ranged from 8.2 percent to 48.8 percent and "distinct ecological differences" within the target area were noticeable. The highest prevalence rates were

found in the most centrally located census tracts and gradually decreased towards the periphery of the study area (Figure 3).

Selected variables were correlated with age- and sex-adjusted rates of elevated diastolic blood pressure. The only variable significantly correlated with hypertension was vacancy rates of urban dwellings ($r = 0.6013$, $p < 0.01$). Correlations with median income ($r = -0.3737$) and median education ($r = -0.3904$) were in the expected direction but were not strongly significant ($p < 0.10$). Although there were no significant correlations with population decreases among different age groups, the trend was considered to be consistent with the concept that urban decay involves the selective out-migration of healthy young adults, leaving the non-mobile, elderly poor behind. In this way,

> the implication of these observations for health planners is a concentration of individuals eligible for high blood pressure management living in decayed central city locations where there is a notorious lack of community-based primary medical care services (Apostolides, 1974, p. 111).

Studies from Africa also indicate that hypertension is more prevalent in urban areas than rural areas. Scotch et al. (1961) reported that a group of South African urban Zulu adults showed a significantly higher incidence of hypertension and significantly higher blood pressure values than a similar group of Zulu adults living in a rural native reserve. When mean blood pressure levels of Zulu were compared with those of blacks and whites from Georgia, Georgia blacks showed the highest mean blood pressure, followed by urban Zulu, Georgia whites and rural Zulu. In Ghana, hypertension has been found to be twice as prevalent in urban areas (8.9 percent)



SOURCE: A. Apostolides et al., "High Blood Pressure: Its Care and Consequences in Urban Health Centers," International Journal of Epidemiology, Vol. 3, No. 2 (1974), p. 110 (reprinted with permission).

Figure 3.--Age and sex adjusted prevalence rates of hypertension among black residents in selected census tracts, Baltimore, Maryland, 1972.

than rural areas (4.5 percent) (Pobee et al., 1977). Analysis of social variables, such as church membership, family structure, and marital status, among urban Zulu indicated that those who maintained traditional cultural practices were more likely to be hypertensive (Scotch, 1963). In this way, Scotch (1963) suggests that the development of hypertension is related to an inability to adapt to the demands of urban living.

Higher rates of hypertension observed in an urban area of Iran compared to coastal and mountain villages support the theory that some aspect of city life is related to hypertension (Nadim et al., 1978). A comparison of blood pressures in three sample populations showed that mean differences in blood pressures between mountain villages, coastal villages and Pahlavi City were statistically significant from $p < 0.05$ to $p < 0.01$ (Table 10). Hypertension rates were also higher in the city (30.5 percent) than in the coastal villages (19.8 percent) or mountain villages (6.6 percent). The average weight of city residents was significantly higher, but even when weight was controlled for, differences between mountain villages and the city were statistically significant from $p < 0.01$ to $p < 0.05$ in each age-sex group. Thus, despite the fact that these population samples contained residents of the same ethnic origin (Guilan) living less than 100 kilometers apart, considerable rural-urban differences in the prevalence of hypertension were found. Nadim et al. (1978) suggest that such differences may be due to the isolation of mountain villages from city life and/or differences in diet and exercise in urban and rural areas.

TABLE 10.--Mean Systolic and Diastolic Blood Pressure in Three Samples (35 Years and Older) Studied in Guilan, 1973.

Sex	Sample Studied	No. Obs.	Blood Pressure			
			Mean SBP	S.D.	Mean DBP	S.D.
Male	Pahlavi City	202	144.5	23.6	82.5	21.5
	Coastal villages	236	135.7	20.4	72.2	11.8
	Mountain villages	137	124.7	17.3	69.4	9.4
Female	Pahlavi City	348	151.3	29.0	81.7	11.3
	Coastal villages	274	146.0	27.0	79.3	12.8
	Mountain villages	135	133.0	20.7	75.3	11.1

SOURCE: A. Nadim et al., "Comparison of the Prevalence of Hypertension in the Rural and Urban Areas of Guilan Province, Northern Iran," Acta Cardiologica, Vol. 33, No. 1 (1978), p. 33.

In summary, distinct regional patterns of hypertension exist in the United States and in other areas of the world. The findings presented here suggest that a number of environmental variables, in addition to genetic factors, may contribute to the development of hypertension. Preliminary epidemiologic studies such as those discussed above have created a wide range of possible etiologies, implicating, among others, physical environment, lifestyle, diet, stress and modernization as possible causes of hypertension. A discussion of these factors follows.

IV. ETIOLOGIES OF HYPERTENSION

A causal relationship between hypertension and some factor or factors has yet to be firmly substantiated. Results from prevalence studies such as those discussed in Section III have generated numerous hypotheses concerning the probable cause or causes of hypertension. A variety of genetic and environmental etiologies have been proposed and there now seems to be some general agreement that both factors may contribute to the development of hypertension. This section includes a review of genetic and environmental variables associated with hypertension. Selected genetic studies are presented first and are followed by selected studies of environmental factors.

Genetic Etiologies

A family history of hypertension is a strong indication that an individual will develop hypertension. The exact mechanisms of heredity's involvement in hypertension is unclear but familial aggregation of blood pressure in children and adults has been demonstrated in many studies. For example, blood pressures of natural children are more similar to those of their families than blood pressures of adopted children are to their families (Smith, 1977). Studies have also shown higher correlations of blood pressures

among monozygotic twins than with other relatives, implicating genetic determinants of familial aggregation (Smith, 1977).

Ethnic differences in blood pressure values have been attributed to physiological correlates of ethnicity such as skin color. The high prevalence of hypertension in the American black population compared to the American white population led to an investigation of such a relationship. In Charleston County, South Carolina, the reflectance of skin color among a black population was measured in order to estimate the degree of skin pigmentation (Boyle et al., 1967). Significant differences in the age-adjusted blood pressures of blacks by skin color were reported. For men, age-adjusted mean systolic blood pressure increased 3.1 mm Hg and mean diastolic blood pressure increased 1.3 mm Hg with each five unit decrease in skin reflectance. In other words, higher blood pressures were positively associated with darker skin color. For females, each five unit decrease of skin reflectance showed an increase of 1.2 mm Hg mean systolic pressure and 0.5 mm Hg mean diastolic pressure. These differences were highly significant in both sexes (Boyle et al., 1967). There was also a very significant difference in mean ages between the darker one-third and the lighter one-third of the black population. The mean age of the darker one-third of the population was 45 years for males and 48 years for females; the mean age of the lighter one-third was 52 years of age for both males and females. Boyle et al. speculated that the age differences could be the result of a higher survival rate for blacks

with lighter skin or a physiological decrease in skin pigmentation with age.

The association of hypertension with skin color may be phychosocial rather than physiological, however, as skin color is related to opportunities for employment, education, mobility and social status in general (Keil et al., 1977). A ten-year follow-up study of black males in Charleston County, South Carolina found that when social class was examined as a controlling factor, the association of hypertension and skin color was greatly reduced (Keil et al., 1977). Age-adjusted incidence of hypertension was 3.8 times higher in lower than upper social class blacks and the difference in incidence rates between dark-skinned and light-skinned blacks was not statistically significant.

The relationships between skin color, blood pressure, socioeconomic level and stress were further examined among white and black populations in Detroit (Harburg et al., 1978, I and II). Nurse interviewers rated skin color on a four-point scale and subjects were grouped according to their ethnic background. Samples were chosen from designated high and low stress areas, based on measures of economic deprivation, residential instability, family instability, crime and density. Partial correlations of nine variables, in addition to skin color, were determined by the least squares regression method.

Darker skin color in black males was significantly related to diastolic pressure ($r = 0.25$, $p < 0.01$) and to systolic pressure at a weaker level ($r = 0.14$, $p < 0.05$). This linear relationship

was shown to be independent of the nine control variables (age, height, weight, smoking status, parental hypertension, educational level, family income, season of the year, and respondent tension) and stressor areas (Harburg et al., 1978, I). For females the relationship was linear but not significant. With age and weight controlled for, residence in high stress areas was related with borderline significance to blood pressure levels in males 25-39 years of age, regardless of skin color. For males 40-59 years of age, however, darker skin color was significantly related to blood pressure, regardless of stress area. The authors suggest that high blood pressure in older blacks with darker skin color may be attributed to suppressed hostilities and their inability to adapt to their social-cultural environment regardless of residential area. Gene admixtures may also be responsible for blood pressure levels, especially when combined with "socially induced stress" (Harburg et al., 1978, I).

Among whites, lighter skin color was associated with higher blood pressure but the magnitude of the association was not significant (Harburg et al., 1978, II). European ethnic background, categorized by a skin color cline in Europe from Northern areas to the Mediterranean, was significantly associated with skin color. Subjects of Mediterranean ethnic origins, with darker skin color, had the lowest blood pressures, and those with Northern European backgrounds, and lighter skin color, had the highest blood pressures, independent of age, weight, height, smoking status, parental hypertension, education, income, season, rated tension, and high and low

stress areas. The authors suggest that cultural differences in response to stress may be manifested physiologically in the form of blood pressure regulation. Specific genetic differences in physiological mechanisms among various ethnic groups may also explain blood pressure variations. The fact that older age and colder season were significantly related to high blood pressures for Northern Europeans but not for Mediterraneans suggests that thermo-regulatory mechanisms may be involved (Harburg et al., 1978, II).

A theory recently proposed by researchers at the University of Indiana suggests that differences in hypertension rates between American blacks and whites may be explained by physiological differences in salt-retention capabilities (Citizens for the Treatment of High Blood Pressure, 1979). According to this theory, black Africans, subsisting on low-salt or salt-free diets, developed a kidney system that could process salt slowly enough to balance the loss of salt through perspiration and thus cope with chronic sodium deficiency. The high-salt intake of the average American diet results in increased blood volume and arterial pressure levels which help the kidneys process sodium more efficiently; persons with a reduced capacity to process sodium may therefore be more susceptible to hypertension (Tobian, 1978). In this way, American blacks may have inherited a physical adaptation that enabled their African ancestors to survive in tropical climates but which is maladaptive for blacks living on a high-salt diet in the United States.

The underlying causes of ethnic differences in blood pressure are open to a variety of interpretations. Eyer (1975) has stated that although the influence of heredity on blood pressure values has been demonstrated, only 20 percent of the variation in phenotypes in a population can be accounted for by heredity of some sort. This heritability estimate was reportedly derived from quantitative examinations of relatives of hypertensives, including identical and fraternal twins. In addition, a review of international epidemiological studies has confirmed that "even with the inclusion of many significant factors correlated with BP, less than 20% of the variation of casual BP in the population can be explained" (Kesteloot and Joossens, 1978, p. 69). Hypotheses involving numerous environmental influences on blood pressure have therefore been proposed.

Environmental Etiologies

Environmental variables implicated in the development of hypertension are diverse and include components of geophysical environments, socio-cultural environments and personal environments.

Lifestyle

Although socio-cultural context often influences personal lifestyles, variables associated with individual habits or practices are considered separately. The environmental factors discussed in this category include those that can be changed by individual decisions and actions.

A factor that shows some of the strongest and most consistent associations with hypertension is obesity. Studies show that obese subjects with normal blood pressures are more likely to develop hypertension than normal or underweight normotensives (Smith, 1977). In addition, hypertensive subjects are at a greater risk of becoming overweight compared to normotensive subjects. Experimental evidence has also demonstrated that a weight loss of 20 pounds is capable of reducing diastolic blood pressure 4 mm Hg (Smith, 1977). In a nationwide screening of one million people, prevalence rates of hypertension were 50 percent to 300 percent higher in the group classified as overweight than in the other normal and underweight groups (Stamler et al., 1978). Furthermore, the relative frequency of hypertension with overweight was larger with each higher degree of blood pressure elevation.

These findings suggest that weight is an important factor in hypertension, possibly even causative in nature. If this assumption is correct, "a sizeable potential exists for lowering the prevalence of hypertension in the population and decreasing its serious consequences through prevention and control of overweight" (Stamler et al., 1978, p. 1610).

Particular dietary patterns are also associated with hypertension. A study of nomadic pastoralists in Kenya, whose diets consisted mainly of milk, meat and blood, exhibited blood pressure levels similar to Europeans up to the age of 40 but thereafter showed no increase with age (Shaper, 1967). Upon entering the army, a group of nomadic warriors changed from a carbohydrate-free diet

to one in which half of their total caloric intake was from carbohydrates. Examinations of the warriors two to three years after living in this "altered environment" showed a rise in blood pressure (Shaper, 1967).

Increasing prevalence rates of hypertension among Papago Indians in Arizona have also suggested that diet is a factor (Strotz and Shorr, 1973). Before World War II, hypertension was not a noticeable health problem among this population. The Papago diet at this time was mostly meat (from hunting or cattle-raising), beans and some desert plants. After World War II, however, a cash economy developed on the reservation and the diet changed to a high carbohydrate diet of beans, wheat flour, potatoes and corn, with liberal use of salt and lard. Simultaneously, the amount of physical labor decreased as hunting and cattle-raising activities decreased. Strotz and Shorr (1973) suggest that these factors may have contributed to the high prevalence of hypertension, some 20 percent, recently observed among Papago Indians living in Arizona.

Salt is one dietary component which has demonstrated consistent associations with hypertension. Studies of populations with low and high salt intakes show marked differences in blood pressure levels with age (Table 11). Although these studies are not adjusted for weight or age, they do suggest that a relationship exists. The relationship between salt and hypertension in laboratory animals has been shown to be direct and unequivocal (Weinsier, 1976). Experimental studies have established that: (1) the amount of salt intake is directly proportional to the severity of hypertension;

TABLE 11.--Salt Intake and Blood Pressure Elevation in Different Populations, by Age.

Population	SBP* (mm Hg) 20-29 years	40-49 years	60-69 years	Dietary Salt
Brazil (Carajas)	107	100	109	No salt, use lyes of vegetable ash (K salts)
New Guinea (Murapins)	126	126	123	0.6 g (24-hour urine)
Botswana (Kung bushmen)	119	116	122	2.0 g (24-hour urine)
Cook Islands (Pukapukas)	113	116	125	2.9-4.1 g (24-hour urine)
United States	119	130	149	±10 g/24 hours
Portugal	126	134	155	not measured
Sweden	125	138	159	not measures
Belgium	132	143	163	4 to 20 g (24-hour urine)
Cook Islands (Rarotongas)	124	151	165	7.0 to 8.2 g (24-hour urine)
Norway	130	141	167	not measured
Wales	120	138	169	8.0 g (24-hour urine)
Bahama Islands (Negroes)	129	154	176	15 to 30 g (24-hour urine)

SOURCE: J. V. Joossens, "Salt and Hypertension, Water Hardness and Cardiovascular Death Rate," Triangle, Vol. 12, No. 1 (1973), p. 10.

*SBP = Systolic Blood Pressure

(2) the younger the age at which a high salt diet is introduced results in a greater sensitivity to development of rapid hypertension; and (3) transient exposure (two to six weeks) to high salt intake in early life can produce permanently elevated blood pressure.

Although a normal person requires only 0.5 g salt or less per day, salt consumption in the United States ranges from 3 g to 30 g, with the majority consuming 7 to 15 g (Weinsier, 1976). Much of this intake is in the form of canned and frozen foods which many people are not aware of. Baby foods, which are heavily salted, expose infants to many times their nutritional requirement. Since the taste for salt is acquired over time, it would seem prudent to avoid such foods whenever possible. If salt is indeed a causative agent of hypertension, it would be possible to reduce the morbidity and mortality in a relatively simple and economical manner (Joossens, 1973).

Other variables of personal lifestyles associated with hypertension include cigarette smoking and alcohol consumption. Data comparing blood pressures of alcohol drinkers and non-drinkers suggest that three or more alcoholic drinks per day is a risk factor for hypertension (Klatsky et al., 1977). The mean difference of men consuming three or more drinks per day and non-drinkers was 10.86 mm Hg ($p < 10^{-24}$). In women the mean difference of those consuming six or more drinks per day and non-drinkers was 5.39 mm Hg ($p < 10^{-6}$). However, blood pressures of men taking two or fewer drinks per day were similar to those of non-drinkers. For women, two or fewer drinks per day resulted in slightly lower pressures than non-drinkers.

Hypertension was much more prevalent among persons having six or more drinks per day than among non-drinkers (Table 12). All associations of blood pressure existed independently of age, race, smoking, coffee use, former heavy drinking, education and obesity (Klatsky et al., 1977).

Smoking, which is a risk factor for several other diseases, seems to have an inhibitive effect on blood pressure. Lower mean blood pressures and body weight values were found in cigarette smokers compared with non-smokers or former smokers (Seltzer et al., 1974). Follow-up after a five-year period showed that those who had quit smoking experienced sharp rises in blood pressure--even those who lost considerable weight. On the other hand, diastolic blood pressures of smokers failed to increase--even in those who gained weight. These associations were controlled for age and body weight.

In summary, these aspects of lifestyle are related to the development of hypertension in individuals. Of course, personal habits are usually influenced by the larger social and cultural context in which they exist. These broader types of environmental influences are examined next.

Socio-Cultural Variables

It is hypothesized that hypertension's association with socio-cultural variables operates through stress mechanisms. Numerous studies have shown increases in blood pressure and prevalence rates of hypertension in populations subjected to stressful situations, whether real or perceived.

TABLE 12.--Prevalence of Hypertension in Heavy Drinkers and Non-Drinkers, by Race and Sex.

	Prevalence of Hypertension			
	White		Black	
	Male	Female	Male	Female
Heavy Drinkers (6 or more drinks)	11.21%	11.27%	15.14%	24.18%
Non-Drinkers	4.61%	6.30%	10.18%	14.71%

SOURCE: Klatsky et al., "Alcohol Consumption and Blood Pressure," New England Journal of Medicine, Vol. 296, No. 21 (1977), p. 1196.

According to Smith and Sing (1977), data suggest that life crises which generate stress may affect blood pressure levels of persons genetically predisposed to hypertension. Thus, unfamiliarity, discomfort, or any kind of change in the cultural, social or economic milieu may precipitate stress which is manifested in a biological manner--in the form of elevated blood pressure.

Comparative population studies of "primitive" and "modern" societies suggest that urbanization and the development of Western lifestyles influence blood pressure levels and the development of hypertension. For example, death rates for diseases associated with hypertension, particularly coronary heart disease, are generally two to three times lower in underdeveloped countries than in developed countries (Eyer, 1975). Cerebrovascular death rates in Canada and Ireland are similar to those of American whites but Japan, a highly urbanized country, has higher rates and Mexico, a less developed country, has lower rates than the United States (Nefzger et al., 1973).

Lovell (1967) compared the mean blood pressures of various ethnic groups, including New Guinea Highlanders, Kalahari bushmen, Pacific Islanders, South American Indians, Australian aborigines, and African nomadic tribesmen. Many of the Pacific Island populations showed lower mean blood pressures than Westerners and the rise of blood pressure with age that occurs in Europeans was absent in these populations. In some population samples in New Guinea, mean blood pressure values actually decreased with age.

One explanation for these variations is that when populations experience some kind of environmental change, mean blood pressure levels rise and at some critical level of acculturation the blood pressure starts to rise with age (Seftel, 1978). In this regard, diet is often implicated in the development of hypertension. Serum cholesterol levels, which influence arterial pressures, are low in most underdeveloped countries but the acceptance of Western lifestyles is associated with an increase in serum cholesterol concentrations. Thus, although Eskimos are known for their low serum cholesterol values, despite a very high-fat diet, most Eskimos in Alaska and Canadian Eskimos living in Montreal have serum cholesterol values at least as high as the white population (Shepard, 1974). Increasing urbanization in Alaskan settlements is also associated with an average 6 to 12 mm increase in skinfold thickness among Eskimos (Shepard, 1974).

Other aspects of modernization may also be involved. The dissolution of the nuclear family, mass unemployment, migration, and the rapid rate of technological and organizational change are generally considered stress-producing experiences (Eyer, 1975). Studies of migrant populations have shown that cultural, social and economic mobility are associated with elevation of blood pressure (Smith and Sing, 1977). In this way, stress is attributed to problems encountered while adapting to unfamiliar environmental situations.

A study of persons who migrated to the city of Teheran from rural parts of Iran (Azarbaijan) showed significantly elevated

blood pressures (Nadim et al., 1978). The prevalence of hypertension in rural areas was much lower compared to migrants and non-migrants living in Teheran and the difference was statistically significant ($p < 0.05$). There was no significant difference in blood pressure levels of migrants and non-migrants living in the city. Body build was associated with hypertension but even when ponderal index, a measure of obesity, was controlled for, differences were not due to obesity alone (Table 13).

A study of migrants living in New Zealand tested the hypothesis that migrants who experience incongruity between their personal values and interaction with a new society will experience greater elevations in blood pressure than migrants who experience no such incongruity (Beaglehole et al., 1977). Migrants from Tokelau, a culturally and geographically isolated island with a subsistence economy, had two blood pressure measurements taken and were assigned a social interaction index derived from five main variables: (1) ethnic affiliation of co-workers, (2) ethnic affiliation of friends with whom leisure time was spent, (3) club and association memberships, (4) degree of participation in Tokelauan community functions and (5) religious affiliation. In this way, social interaction was viewed as the extent to which the migrants reacted with others outside the Tokelauan migrant community. Age-adjusted, sex-specific blood pressures of Tokelauan adults showed a significant positive association between elevated blood pressure and the degree of social interaction.

TABLE 13.--Hypertension by Age, Sex, and Ponderal Index in Samples Studied in East Azarbaijan and Teheran City.

Sex/Age	Sample Studied	Ponderal Index: Obese No. Ob.	Obese % Hyp.	Normal/Thin No. Ob.	Normal/Thin % Hyp.	All No. Ob.	All % Hyp.
Male 40-49	Rural	28	7.1	85	7.0	113	7.1
	Migrant Az	63	12.7	45	13.3	108	13.0
	Urban non-migrants	32	21.9	18	0.0	50	14.0
	Migrant Other	21	38.1	15	6.7	36	25.0
Male 50-59	Rural	23	13.0	40	5.0	63	7.9
	Migrant Az	48	29.2	46	13.3	94	22.3
	Urban non-migrants	42	35.7	25	16.0	67	28.4
	Migrant Other	27	37.0	13	15.4	40	30.0
Female 40-49	Rural	57	17.5	72	15.3	129	16.2
	Migrant Az	94	26.6	18	0.0	112	22.3
	Urban non-migrants	116	25.9	18	5.6	134	23.1
	Migrant Other	107	33.6	26	7.7	133	28.6
Female 50-59	Rural	27	29.6	47	8.5	74	16.2
	Migrant Az	78	47.4	11	9.1	89	42.7
	Urban non-migrants	90	33.3	16	12.5	106	30.2
	Migrant Other	62	48.4	18	22.2	80	42.5
All	Rural	135	17.0	244	9.4	379	12.1
	Migrant Az	283	29.7	120	10.9	403	24.3
	Urban non-migrants	280	29.3	77	9.1	357	24.9
	Migrant Other	217	38.7	72	12.5	289	32.2
	TOTAL	915	29.8	513	10.1	1428	22.7

SOURCE: A. Nadim et al., "Blood Pressure and Rural-Urban Migration in Iran," International Journal of Epidemiology, Vol. 7, No. 2 (1978), p. 138.

Increased social interaction with the New Zealand society was able to explain 1.4-2.3 percent of the total variance in blood pressure; body mass and length of stay in New Zealand accounted for 7.1-11.0 percent of the variance (Table 14). Although increasing levels of interaction with a new society may change lifestyles and result in increased levels of blood pressure, a causal relationship between hypertension and social interaction was not established. The decision to emigrate might indicate that an individual has problems adapting to the social-cultural environment in which he/she lives (Smith and Sing, 1977). Therefore, those who migrate may have a high risk for developing hypertension even before they interact with another society.

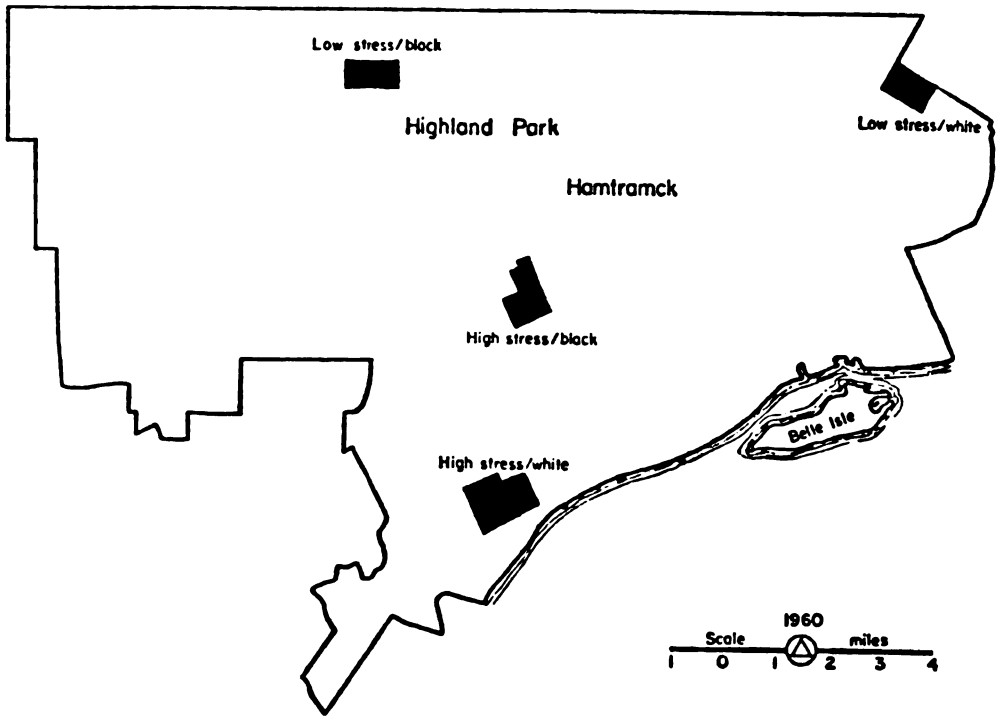
Stress is also produced by various types of social and economic deprivation. In many instances, the distribution of blood pressure values among different ethnic groups is associated with such socio-economic variables. For example, although mean blood pressures are generally lower in underdeveloped countries, some populations living in underdeveloped societies that evolved under oppressive conditions (such as the Caribbean) have high average blood pressures (Eyer, 1975). Blacks living in the United States and in the West Indies have higher blood pressures than blacks living in Liberia, historically a principle source of black migration to the Western hemisphere (Dawber et al., 1967). Also, blood pressures of migrant Zulu adults living in urban areas of South Africa under apartheid policy are higher than blood pressures of Zulu living in rural areas (Scotch, 1963).

TABLE 14.--Proportions of Explained Variance in Blood Pressure Z-Scores by Sex.

Sex		Variance Attributed to: Body Mass and Length of Stay in New Zealand (%)	Variance Attributed to: Social Interaction (%)
Males	Systolic	7.1	2.1
	Diastolic	11.0	2.3
Females	Systolic	10.2	1.4
	Diastolic	10.4	1.9

SOURCE: R. Beaglehole et al., "Blood Pressure and Social Interaction in Tokelauan Migrants in New Zealand," Journal of Chronic Disease, Vol. 30 (1977), p. 811.

The association of residence in stressful areas with hypertension was examined among blacks and whites living in Detroit (Harburg et al., 1973). Census tracts were assigned high and low stressor scores based on socio-economic status indicators and instability scores derived from variables of economic deprivation, residential instability, family instability, crime and density. Predominantly white and predominantly black high and low stress areas provided the sample population (Figure 4). Measurements of blood pressure revealed that males in the high stress/black areas had significantly higher proportions of borderline and definite hypertension (38 percent) than males living in low stress/black areas (19 percent), $p < 0.01$. There was no significant difference between whites living in high and low stress areas. When the results were controlled for age, overweight, ponderal index, time of day, hours since last meal and rated tension at time of readings, the differences between high and low stress areas were reduced. Mean blood pressures of black males from high and low stress areas were still significantly different. White females from high stress areas also showed significantly higher systolic pressures than those from low stress areas. Furthermore, blacks in low stress areas did not differ in levels of blood pressure from whites in low stress areas. The results of this study are debatable, however, as significant correlates of blood pressure, such as income, education, diet and familial hypertension, were not controlled on an individual basis. The effects of residential stress on hypertension, therefore, have yet to be clearly demonstrated.



SOURCE: E. Harburg et al., "Sociological Stressor Areas and Black-White Blood Pressure: Detroit," Journal of Chronic Diseases, Vol. 26 (1973), p. 598 (reprinted with permission).

Figure 4.--Black and white stressor areas in Detroit.

Stress created in the work environment is also associated with elevations in blood pressure. Noise is one such occupational hazard. A study of textile mill workers in Iran exposed to an average noise level of 96 decibels, showed that the weavers had a significantly greater risk of developing hypertension when compared to a group of weavers matched for similar socio-economic conditions who were working in light industries without exposure to an intensive noise level (Parvizpoor, 1976). Among 821 weavers, 8.5 percent had definite hypertension and 12.4 percent had borderline hypertension. Of 412 control subjects, 2.4 percent had hypertension and 4.6 percent were borderline hypertensives. The difference was significant at $p < 0.01$. Higher prevalence rates in the weavers appeared at relatively young ages (30-39 years) and increased with length of employment in the mill.

Similar findings were reported among 200 male industrial workers in Sweden tested for hearing loss (Jonsson and Hansson, 1977). Average blood pressures were significantly higher in subjects with noise-induced hearing losses than in subjects with normal hearing; however, no control variables were considered in this study. The investigators stated that, although a causal relationship between noise and blood pressure was not proven, repeated elevations of blood pressure due to noise stress may cause a permanent rise in blood pressure due to structural adaptation of the heart and resistance vessels. A follow-up of the preliminary findings, with more detailed examinations, has been planned. It is hoped that control subjects

will be matched for variables such as age, weight, sex, race and heriditary characteristics.

Exposure to high temperatures is another variable which may be associated with hypertension. An investigation of the working conditions of foundry workers in Brazil showed that continued exposure to high levels of heat was signicantly associated with higher prevalence rates of hypertension (Kloetzel et al., 1973). No conclusions can be drawn from this study, however, since there was no matched group of controls and little quantitative analysis of the data.

Although the effects of stress on physiologic changes in blood pressure have been demonstrated in numerous ways, there is much debate on the precise nature of hypertension's association with stress (Marx, 1977). For those who view stress as a result of modernization, "major social changes are necessary to prevent modern hypertension" (Eyer, 1975, p. 550). Others view stress in terms of the "interaction between a particular external environment and a particular kind of person" (Marx, 1977, p. 907). This kind of genetic-environmental viewpoint supports hypertension control measures aimed at identification of "individuals of high and low environmental and biological risk" (Smith and Sing, 1977, p. 789). Environmental risk factors in the geophysical environment that have been associated with hypertension are examined next.

The Geophysical Environment

The geophysical environment refers to those geologic, hydrologic and chemical components that exist within defined areas. Three kinds of variables from the physical surroundings have demonstrated relationships with hypertension--altitude, water hardness and trace metals.

High elevations of altitude seem to have a protective effect against hypertension. A comparison of five small communities in Peru revealed that the age-adjusted prevalence of systolic hypertension in males was twelve times higher in the two communities at sea level than in the three villages at altitudes above 13,000 feet (Ruiz and Penaloza, 1977). The difference was significant at $p < 0.001$. Diastolic pressures were also higher at sea level but at a lower level of significance ($p < 0.05$ to 0.001).

Further analysis showed that:

1. blood pressures of natives living at high altitudes increased after prolonged residence at sea level and tended to resemble the pressures of persons living at sea level.

2. retrospective observation of 100 white males originally from sea level residences showed that their blood pressure values decreased after living from 2 to 15 years at an altitude of 12,400 feet.

3. at sea level, hypertension is more frequent in females and systolic hypertension is more common than diastolic hypertension whereas at high altitudes, hypertension is more frequent in men and diastolic is the more common type of hypertension.

The diet of populations living at high altitudes such as the Andes Mountains is suggested as one possible explanation for these

differences. The Andean diet is high in carbohydrates and vegetable proteins and is noted for its high mineral content, especially zinc and other trace elements (Ruiz and Penaloza, 1977). Physiological differences have also been observed in mountainous areas. Hypoxia, which determines functional and structural vascular changes, is a chronic condition at high altitudes and it is hypothesized that this may improve the supply of blood oxygen to tissues (Ruiz and Penaloza, 1977). In this way, some kind of biological-environmental interaction may be responsible for blood pressure variations at different altitudes.

An examination of changing hypertension rates in different regions of Colorado has also suggested that altitude may be a factor. Mean annual rates of hypertension and hypertensive heart disease for 1949-51 and 1959-61 decreased by one-half to one-third in all regions of Colorado except one--a band of counties on the high plains lying at an altitude of 3,500-4,000 feet (Morton, 1970). There were no known differences in the socio-economic status or the availability of medical resources among these areas which could be attributed to the differences in hypertension prevalence.

A survey taken among selective service registrants in Colorado showed that rates of hypertension were highest in the lowest altitude stratum and that there was an inverse relationship between altitude and hypertension rates (Table 15). These rates should be viewed with caution, however, since the number of hypertensives at high altitudes was very small. The differences could not be explained by different ethnic compositions of the regions

TABLE 15.--Prevalence of Hypertension Among Colorado Selective Service System Registrants.

Mean Population Elevation (ft)	Registrants Listed		Hypertension	
	Total	(% with Known BP)	Number	Rate/ 1,000
8,000 - 10,152	468	(34.2)	2	4.3
7,000 - 7,999	1,939	(34.2)	7	3.6
6,000 - 6,999	4,423	(30.2)	25	5.7
5,000 - 5,999	18,025	(32.4)	135	7.5
4,000 - 4,999	7,167	(34.5)	81	11.3
3,489 - 3,999	1,142	(36.5)	25	21.9
TOTAL	33,484	(32.9)	275	8.2

SOURCE: W. E. Morton, "Geographic Pattern of Hypertension in Colorado," Archieves of Environmental Health, Vol. 20 (1970), p. 693.

but levels of education, income, occupation and urbanization which differed in parts of Colorado, may account for some of the altitude effects (Morton, 1970).

Numerous other studies have established a relationship between water quality and hypertension morbidity and mortality. In 1950, death rates from hypertensive heart disease in the United States were found to be inversely proportional to water hardness ($r = -0.57$, $p < 0.01$), based on the total calcium and magnesium concentrations in parts per million (Perry and Perry, 1974). Although a study of hard water towns and soft water towns in Great Britain reported a correlation of -0.22 for water hardness and death rates from hypertensive heart disease in 1951, the correlation coefficient for all cardiovascular diseases was -0.54 in 1951 and -0.65 in 1961 (Perry, 1972).

Analysis of changes in the water supply in England and Wales between 1925 and 1955 showed that in towns where the water supply became softer, mortality from cardiovascular disease increased 20 percent, compared with an 8.5 percent increase in cardiovascular deaths in towns where the water supply became harder (Table 16). In towns where no change in water supply occurred, cardiovascular death rates increased 11 percent (Perry, 1972).

Areas in Japan with greater acidity in river water were associated with higher mortality rates from stroke ($r = 0.63$) and higher rates of heart disease ($r = 0.67$) (Schroeder and Kraemer, 1974). In the United States, alpha-radioactivity was used as a measure of water quality in two hard-water river basins and two

TABLE 16.--Mean Percentage Changes in Death Rate from 1951-1961 as Function of Change in Water Hardness.*

Causes of Death	Hardness of Drinking Water		
	Increased (5 towns)	No Change (72 towns)	Decreased (6 towns)
Cardiovascular	8.5	11.2	20.2
Other	-10.8	-13.0	-12.4

SOURCE: H. M. Perry, Jr., "Hypertension and the Geochemical Environment," Annals of the New York Academy of Sciences, Vol. 199 (1972), p. 211.

*Values are percent changes in death rates in England and Wales over a 10-year period for males 45-64 years of age. Similar trends are seen for women and for older men.

soft water river basins (Perry, 1972). Death rates from hypertension and ischemic heart disease among 7.5 million people living in 140 counties along the Ohio, Columbia, Missouri and Colorado rivers were compared. As Table 17 shows, death rates, except those from non-cardiovascular disease, decreased as alpha-radioactivity increased. Comparing the Colorado and Ohio river basins, death rates from hypertensive heart disease and ischemic heart diseases were 41 percent and 25 percent lower, respectively, along the Colorado River, which contains the hardest water.

The substance in hard water that appears to protect against cardiovascular deaths has yet to be determined. Analysis of 36 components of municipal water supplies failed to disclose any single element or quality that might influence vascular death rates (Schroeder and Kraemer, 1974). Water considered to be partially protective contains alkali metals (lithium, sodium, potassium and rubidium), alkali earths (magnesium, calcium, strontium and barium) and essential trace metals vanadium and molybdenum, along with uranium, boron, silicon and chloride, sulfate and bicarbonate anions (Schroeder and Kraemer, 1974). This study suggests that it may be more beneficial to investigate the corrosiveness of soft water (which dissolves elements such as copper, cadmium, zinc, lead and antimony from water pipes) than water hardness as an influence of hypertension morbidity and mortality.

One trace element that has recently aroused suspicions of involvement in hypertension is cadmium. Experimental results have shown that rats chronically fed small doses of cadmium will develop

TABLE 17.--Death Rates and River Water Radioactivity (Hardness).

River Basin	Alpha Radioactivity (c/l)	Annual Death Rates Per 100,000 Population		
		HHD[a]	IHD[b]	NCVD[c]
Ohio	0.25	40	303	455
Columbia	0.40	33	303	448
Missouri	3.01	28	276	460
Colorado	6.00	23	228	440

SOURCE: H. M. Perry, Jr., "Hypertension and the Geochemical Environment," Annals of the New York Academy of Sciences, Vol. 199 (1972), p. 210.

[a]Hypertensive Heart Disease

[b]Ischemic Heart Disease

[c]Noncardiovascular Disease

hypertension (Perry and Perry, 1974). The relationship between cadmium concentrations and hypertension in humans, however, is less definitive (Perry and Perry, 1974; Ostergaard, 1977). Renal cadmium concentration and prevalence of hypertension show similar geographic distributions in some instances. For example, non-industrialized areas of Africa are associated with low rates of hypertension and low levels of renal cadmium while industrialized areas of Japan show high prevalence rates of hypertension and high renal cadmium concentrations (Perry and Perry, 1974). On the other hand, Ostergaard (1977) found higher renal cadmium concentrations in normotensives than in hypertensive subjects. He suggests that other studies have not always controlled for confounding variables such as age and smoking which may influence results. The quality of drinking water should also be considered in cadmium studies, since hypertension could be influenced by enhanced cadmium uptake in soft water supplies.

In these ways, then, factors of the geophysical environment must be considered as potential contributors to the development of hypertension. Demonstration of causal relationships has been difficult because of the interrelated nature of the variables discussed in this section. For example, higher rates of hypertension found in persons living in urban areas may be the result of high-salt diets, sedentary lifestyles, or an inability to cope with the stresses of modern urban life. Although each variable in itself may not have a strong effect on the development of hypertension, the

synthesis of genetic, dietary and environmental factors may produce an effect capable of raising blood pressure levels. Interdisciplinary research on hypertension, therefore, seems warranted.

V. CONCLUSIONS

Numerous strategies for the prevention and control of hypertension exist. The most common strategy currently in use consists of hypertension screening programs aimed at identification of hypertensive individuals. Aggressive follow-up programs are also being tried in order to improve patient compliance once treatment is initiated. Programs such as those developed by Erfurt and Foote (1976) involve contacting hypertensive individuals and their physicians by phone, mail or visit in order to chart the patient's progress in blood pressure reduction over time.

Some believe that hypertension can only be conquered by a major upheaval in the social structure which will alleviate the stress created by the modern, urbanized world in which we live. Behavioral modification, aimed at changing personal habits and lifestyles, is promoted by others as a way to prevent hypertension. Still another strategy involves environmental modification. This entails making living areas more pleasant (and less stressful) by reducing levels of poverty, crime and crowding and by providing safeguards against harmful chemical agents in food and water supplies.

The complex interaction of physiological, psychological and environmental variables complicates any analysis of hypertension.

Nevertheless, the endemic nature of hypertension in contemporary society makes its analysis necessary. Although hypertensive patients can be told what their chances are of dying from stroke, congestive heart failure or myocardial infarction, physicians are unable to explain in certain terms why certain individuals develop hypertension and others do not. In this paper, various aspects of hypertension are studied with the hope that some cause of the disease may be illuminated and future cases may be prevented.

The current state of the literature on hypertension is quite inadequate. The lack of a standard definition in epidemiological studies is a major problem. Data comparison among hypertension studies, particularly on an international scale, is extremely difficult due to differences in terminology, methods of blood pressure measurement and diagnostic criteria. It is hoped that researchers in the future will make an effort to standardize these aspects of their investigations.

Future studies should also control for the many confounding variables that exist in investigations of hypertension. Many of the earlier studies that fail to control for age, weight, race, socio-economic status and family history should be viewed with caution as their results may be biased.

This paper has demonstrated the many ways in which a geographic perspective can be useful in the study of hypertension. Since the distribution of hypertension has already been quite well-defined on an international level and on a national level in the United States, spatial analyses of hypertension at smaller scales

would provide useful results for health planners. In a time of scarce medical resources, identification of high-risk populations could be greatly aided by geographers. A wholistic approach to the study of human-environmental interactions may unravel some of the etiologic mysteries surrounding hypertension. Integrative models which synthesize hypertension findings from the behavioral and social sciences can be used to facilitate interdisciplinary research of the disease (Stahl et al., 1975). Once high-risk areas and etiologic factors have been adequately identified, strategies to improve health care delivery programs and compliance to treatment regimens can be formulated in a rational and efficient manner.

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