expenditures for the laboratory. Some specialized personnel, both technical and medical, can be contributed by international organizations or the governmental agencies of developed countries. If the pathologist has experience in clinical pathology, as it often happens in the Anglo-Saxon world, he or she can also take care of other laboratory sections. In addition, the pathologist might become involved in teaching intermediate-level personnel.

Conclusion

It is important that a fraction of medical graduates in developing countries be instructed in pathology to constitute a network of laboratories at the regional level. Such effort should yield results in health care and in second- and third-level prevention that fully justify the human and financial resources needed for the laboratories.

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Rocky Mountain Spotted Fever in Georgia, 1961-75: Analysis of Social and Environmental Factors Affecting Occurrence

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Synopsis

For the period of 1961 through 1975, 10 geographic and sociologic variables in each of the 159 counties of Georgia were analyzed to determine how they were correlated with the occurrence of Rocky Mountain spotted fever (RMSF).

Combinations of variables were transformed into a smaller number of factors using principal-component analysis. Based upon the relative values of these factors, geographic areas of similarity were delineated by cluster analysis. It was found by use of these analyses that the counties of the State formed four similarity clusters, which we called south, central, lower north and upper north.

When the incidence of RMSF was subsequently calculated for each of these regions of similarity, the regions had differing RMSF incidence; low in the south and upper north, moderate in the central, and high in the lower north. The four similarity clusters agreed closely with the incidence of RMSF when both were plotted on a map.

Thus, when analyzed simultaneously, the 10 variables selected could be used to predict the occurrence of RMSF. The most important vari-

ables were those of climate and geography. Of secondary, but still major importance, were the changes over the 15-year period in variables associated with humans and their environmental alterations.

Detailed examination of these factors has permitted quantitative evaluation of the simultaneous impacts of the geographic and sociologic variables on the occurrence of RMSF in Georgia. These analyses could be updated to reflect changes in the relevant variables and tested as a means of identifying new high risk areas for RMSF in the State. More generally, this method might be adapted to clarify our understanding of the relative importance of individual variables in the ecology of other diseases or environmental health problems.

DURING THE 1950s, THE REPORTED OCCURRENCE of Rocky Mountain spotted fever (RMSF) in the southeastern United States steadily declined, and some observers predicted that the disease would soon cease to be a significant public health problem. In 1959, however, Smadel predicted that this trend would reverse as man and ticks came into more frequent contact (*1*), and in the 1960s and 1970s, consistent with this forecast, the reported occurrence rose sharply. In 1960 only 1.1 cases per million population were reported for the United States, but by 1977 the reported incidence had reached 5 cases per million population nationally and 16.6 cases per million population in the Southeast (*2*). At the same time, the dynamics of man's involvement in the RMSF cycle in the eastern United States have proved to be extremely complex and elusive.

A number of workers have investigated individual climatologic, geographic, and sociologic variables that appear to be associated qualitatively with the occurrence of RMSF (*3–15*). None of the investigators, however, examined multiple variables simultaneously, and none has attempted to determine the relative quantitative impact of various climatologic and sociologic conditions or changes on the occurrence of RMSF.

In this study, we attempted to identify retrospectively important geographic and sociologic variables which could have contributed to the high rate of RMSF reported in Georgia. Then, we analyzed those variables for which published data were available, using a method designed to measure the relative impact of the most important of the selected variables on disease occurrence. RMSF incidence was not calculated until after the multivariate analysis of the county data had been completed, and similarity clusters of counties were identified. The incidence of RMSF for these county clusters was then calculated to determine if statistically similar county groups were correlated with areas of known disease incidence. Our analysis was thus predictive of areas of higher or lower RMSF risk. If a correlation was found to exist, changes in certain variables over time should enable us to predict new areas of increased risk for RMSF.

Materials and Methods

Case identification and incidence rate. Between 1961 and 1975, 135 cases of RMSF in 80 of the State's 159 counties were reported to the Georgia Department of Human Resource (GDHR) (fig. 1). Records of all cases of RMSF reported to the GDHR for these years were reexamined. To be included in this analysis, a case of RMSF was defined as any illness diagnosed as RMSF and reported by a physician to the GDHR, which had either met acceptable laboratory requirements for the confirmation of RMSF (*2*), or in the absence of laboratory confirmation, sufficient clinical details had been described by the physician to ascertain that the illness occurred between March 1 and November 1 and included fever, headache, and a centripetally spreading rash.

The reported incidence per million in each county was defined to be the total number of reported cases of RMSF during the 15-year study period per total person-years of exposure.

Selection of environmental variables. Rocky Mountain spotted fever is an infection of humans, accidentally and incidentally acquired when people intrude into an area where the zoonotic cycle of transmission of the causative agent, *Rickettsia rickettsii*, persists. The zoonosis in the eastern United States is maintained transovarially in *Dermacentor variabilis* ticks, and through transmission by these ticks to small wild rodents, which, in turn, infect previously uninfected ticks and establish new lines of transmission. Therefore, environmental variables were selected for this study that could conceivably affect populations of

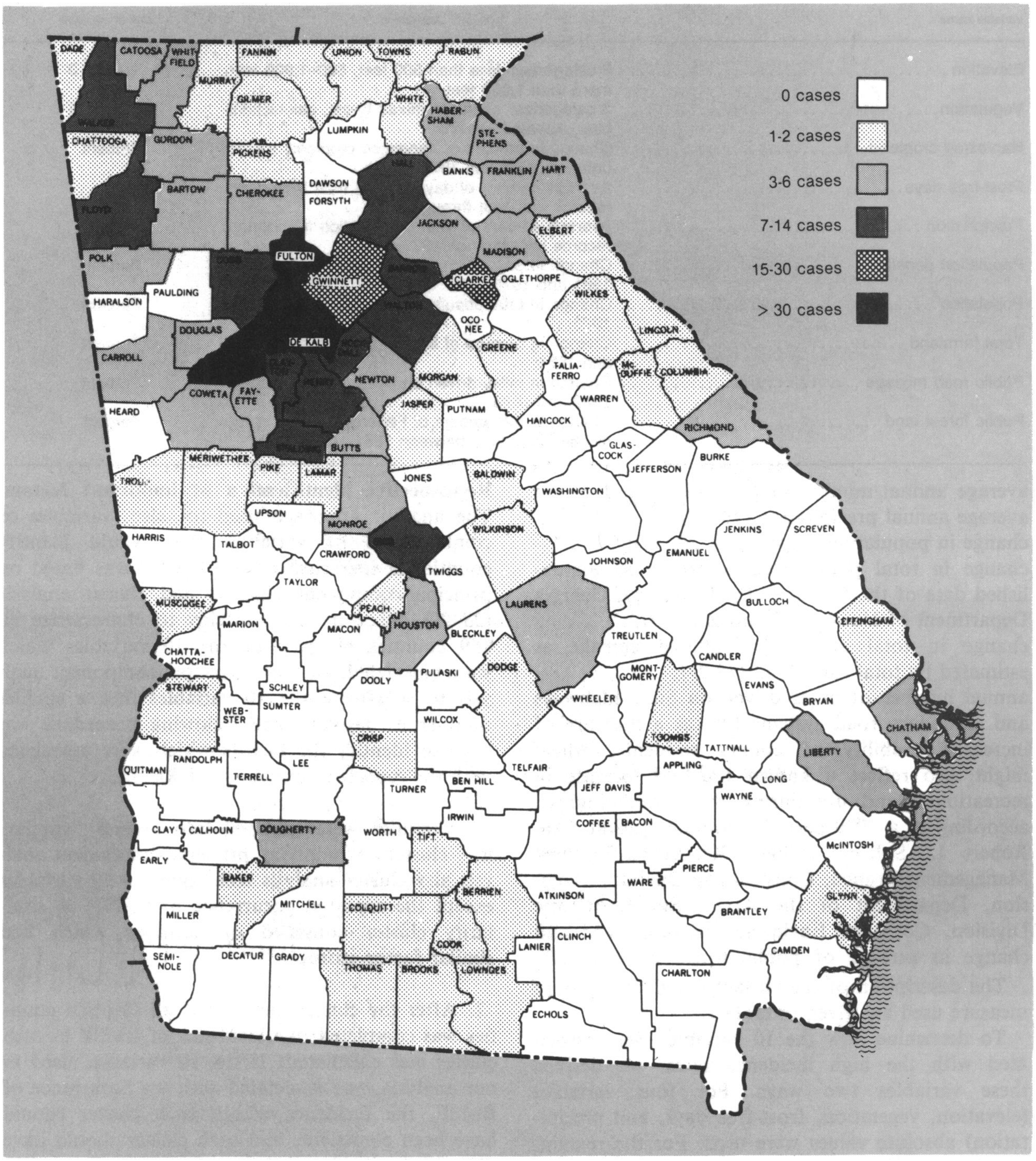


Figure 1. Reported cases of Rocky Mountain spotted fever by county, Georgia, 1961–75.

ticks or their rodent hosts, or reflect changes made by human alterations of natural areas.

From all the variables selected, the number was reduced to 10. Each of these was shown to exert an influence not accounted for by any of the others by using the correlation coefficient matrix with a cutoff value for selection of 0.90. Data routinely collected from each of the 159 counties in Georgia on the following 10 environmental variables were thus included in the analysis:

elevation (*16,17*);
climax vegetation type (*17*);
change in acreage in harvested cropland (*18, 21–23*);

Table 1. Ten environmental variables used in principal-component analysis to describe 159 Georgia counties, 1961–75

Variable name	Description	Unit of measure
Elevation	3 categories: less than 500 feet, 500–1,000 feet, more than 1,000 feet.	1, 2, or 3
Vegetation	3 categories: southern mixed forest, oak-hickory-pine, Appalachian oak.	1, 2, or 3
Harvested cropland	Change in amount of harvested cropland between 1964 and 1975.	Percent
Frost-free days	Average number of days without frost from time records first kept through 1971.	Days
Precipitation	Average amount of total precipitation from time records kept through 1971.	Inches
Population density	Change in population per square mile between 1961 and 1975.	Percent
Population	Change in total population between 1961 and 1975.	Percent
Total farmland	Change in amount of land in farms between 1964 and 1974.	Percent
Public road mileage	Change in miles driven on public roads between 1963 and 1973.	Percent
Public forest land	Change in the amount of Federal, State, and municipal forest land between 1961 and 1972.	Percent

average annual number of frost-free days (*16–18*);
average annual precipitation (*16–18*);
change in population density (*19, 20, 24*);
change in total population, according to unpublished data of the Office of Epidemiology, Georgia Department of Human Resources in 1979;
change in total amount of altered acreage as estimated by total farm land (*18,23*);
annual number of miles driven on State highways and secondary road systems (*25*) as a measure of increased mobility of county residents, which might also reflect a known fourfold increase in recreational land use during the period studied, according to a 1979 personal communication from Robert L. Solheim, Chief, Recreation-Resource Management Branch, Construction-Operation Division, Department of the Army, South Atlantic Division, Corps of Engineers, Atlanta, GA; and change in acreage of public forest land (*26,27*).

The description of the variables and the units of measure used are given in table 1.

To determine how the 10 variables were associated with the high incidence rates, we defined these variables two ways. For four variables (elevation, vegetation, frost-free days, and precipitation) absolute values were used. For the remaining six variables, the percentage change that had occurred between 1961 and 1975 was analyzed (table 1). Since each of the data sources (forestry, agriculture, highways, and so on) published statistical updates at differing times and irregular intervals, precisely concurrent data were not available; all published statistical information covering a major part of the 15-year study period was used.

Retrospective identification of important factors. The analytic approach used to select variables or combinations of variables that would identify counties at increased risk of RMSF was based on principal-component analysis and cluster analysis (*28–29*). Since it was unwieldy to characterize all 159 counties by each of the 10 variables which were correlated, we used principal-component analysis to transform the 10 variables into a smaller number of factors. The following procedure was used to identify the factors which were associated with the reported occurrence of RMSF.

1. Counties were grouped into several "similarity" clusters by applying principal-component analysis and cluster analysis techniques to all variables except the reported occurrence of RMSF. A similarity cluster consisted of counties which had similar factor scores.

2. After the cluster analysis of all Georgia counties was completed, the incidence of RMSF in each cluster was calculated. If the 10 variables used in our analysis were associated with the occurrence of RMSF, the incidence within each cluster should have been consistent, and each cluster should have differed in incidence from all other clusters. In other words, incidence should vary greatly for counties assigned to different similarity clusters but not for counties within the same similarity cluster.

3. These factors were then examined to determine the relative importance of their component variables.

Following is a description of the methods we used in the statistical analysis.

Principal-component analysis. Principal-component analysis allows most of the variation in a multivariate system to be summarized in fewer new variables, which are called factors. The factor which accounts for the greatest amount of the total variance of the multivariate data is defined as the first factor. If A, B, C, D, E, F, G, H, I, and J are 10 measurements of particular variables (elevation, precipitation, and so on), the first factor of the 10 measurements of these variables is the linear function

$$Y_1 = a_1 A + a_2 B + a_3 C + \ldots + a_{10} J,$$

where $a_1, a_2, \ldots, a_{10}$ are coefficients.

The second factor of the 10 measurements of the same variables is that linear compound

$$Y_2 = b_1 A + b_2 B + b_3 C + \ldots + b_{10} J,$$

where $b_1, b_2, \ldots, b_{10}$ are coefficients. The second factor accounts for the second largest percentage of the total variance.

The third and all the other factors up to the tenth are defined in the same manner.

One technical advantage of the principal-component analysis is that it does not put any restrictions on kinds of measurements. Measurements could be absolute values of some physical measurements or their ratios (*29*).

In this study, each county is given 10 factor values that are derived from measures of the raw data of 10 variables using a principal-component analysis computer software package. The first two factors explain 57 percent of the total variance in the data (table 2). Only these were retained in the analysis because the third factor accounts for only 10 percent of the total variation, which is the same proportion as that of a single variable. Since all 10 variables in our study are standardized, the variance of each variable is 1, and therefore each variable accounts for 10 percent of the total variation. Each county can thus be plotted in a two-dimensional space in which two axes are the first two factors when each county is represented by the values of the first two factors.

Cluster analysis. The purpose of this procedure is to create a "pseudo-prospective" study using retrospective data. To illustrate, let us assume that a prospective study is being designed to determine the impact of two factors, 1 and 2, on the reported incidence of RMSF. Then, let us assume that each of the two factors have two values, "high" and "low," creating four clusters of counties which will be called similarity clusters. The first cluster consists of counties with a high value of factor 1 and a high value of factor 2, the second cluster with a high value of factor 1 and a low value of factor 2, the third cluster with a low value of factor 1 and a high value of factor 2, and the fourth cluster with a low value of factor 1 and a low value of factor 2. Within each of the four clusters, counties now have similar values of factors 1 and 2. On the other hand, two counties from two different clusters are dissimilar with respect to these factors.

Table 2. Percent of variation accounted for by factors derived in factor analysis of 10 environmental variables to describe 159 Georgia counties, 1961–75

Factor	*Variation (percent)*
1st	39.2
2nd	17.6
3rd	10.3
4th	8.8
5th	8.1
6th	3.8
7th	4.0
8th	3.3
9th	1.8
10th	1.1

If the two factors, 1 and 2, are significantly related to the reported incidence of RMSF, then the distribution of the reported incidence of RMSF will be different in the four similarity clusters. If the distributions of reported incidence of RMSF are different for the similarity clusters, one may conclude that both factors 1 and 2 are associated with disease occurrence. On the other hand, if the distributions for the four similarity clusters show no significant differences, this would indicate that the two factors are not associated with disease occurrence.

After retrospectively classifying all the counties into four similarity clusters by using the two most important factors determined from the 10 reported variables, the distribution of the reported incidence of RMSF in the four clusters was compared. Application of these methods to the data showed that the reported incidence within each cluster was consistent, and each cluster differed in incidence from all other clusters.

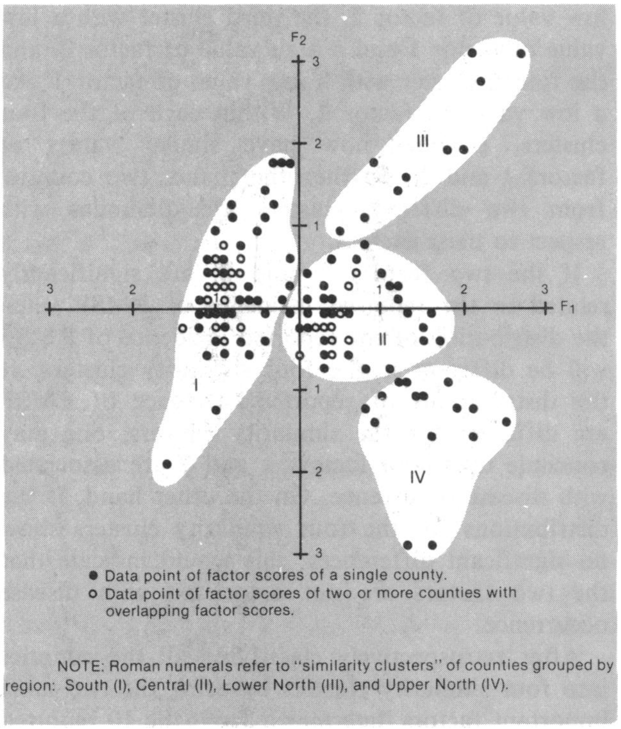
Results

We identified two major factors which characterize the 159 counties in Georgia, each a linear combination of the 10 variables. These two factors

Table 3. Coefficients of ten environmental variables for two factors that best describe 159 Georgia counties, 1961–75

Variable	*Factor 1*	*Factor 2*
Elevation	.2362	-.1053
Vegetation...............	.2187	-.1883
Harvested cropland.......	-.2061	-.0577
Frost-free days...........	-.2044	.2083
Precipitation	.1430	-.2577
Population density........	.1080	.3898
Population................	.1423	.3179
Public forest land	.0199	-.0697
Public road mileage	.0623	.2795
Total farmland	-.1055	-.2740

Figure 2. Plot of social-environmental components of 159 Georgia counties. Each county is plotted in the F_1 - F_2 plane where F_1 is the most important factor defined by 10 social-environmental variables and F_2 is the second most important factor.



NOTE: Roman numerals refer to "similarity clusters" of counties grouped by region: South (I), Central (II), Lower North (III), and Upper North (IV).

accounted for approximately 57 percent of the total variation for the 10 variables, factor 1 accounting for 39.2 percent of the variation, factor 2, 17.6 percent. Ignoring small coefficients, the important variables in factor 1 included elevation, class of climax vegetation, average number of frost-free days, and percent change in amount of harvested cropland. The important variables in factor 2 included average amount of precipitation, percent change in population density, percent change in total population, percent change in miles driven on public roads, and percent change in acreage of total farmland (table 3).

Most of the component variables in factor 1 are climatic-geographic in nature. On the other hand, in factor 2, most of the important variables are related either to humans or their activities. Note that the coefficients of the climatic variables in factor 2 are of the opposite sign of climatic variables in factor 1 (table 3).

The 159 counties in Georgia, which were originally characterized by 10 environmental variables, can now be characterized by the two factors. Because of the statistical properties of the factor analysis, any two counties which are similar in their values of the two factors are also similar in their values of the original 10 county variables.

The 159 counties grouped themselves into four similarity clusters which we have called the south, central, lower north, and upper north, as defined by the two factors or equivalently by 10 environmental variables (fig 2). To illustrate the relationship of the original 10 variables with the incidence rate of RMSF for these four clusters, the average values of the 10 variables are described qualitatively for the four regions delineated by the cluster analysis and compared to the incidence of RMSF calculated subsequently for each of the four regions (table 4).

Note that the highest incidence rate of RMSF is found in the region we called lower north Georgia and is associated with large increases in population density, total population, and miles driven on public roads combined with large decreases in acreage of farm and cropland (table 5). The lowest incidence rate of RMSF, on the other hand, is found in the south Georgia region and is associated with a high value of frost-free days and with low values of elevation, vegetation type, population, change in amount of harvested cropland, very small decreases in acreage of total farmland, and miles driven on public roads. Hence, the two factors, and therefore the original 10 environmental variables, were associated with the reported occurrence of RMSF in Georgia. When the counties in each of the four county clusters were plotted on a State map, we note that the four county clusters correspond to four geographic regions (fig 3). When the counties that actually had reported the occurrence of RMSF were then compared with the four regions developed by the county cluster analysis, there was very close agreement. Since the cluster analysis was based upon county similarity, the four clusters contain, of course, counties which had not reported any cases of RMSF.

Table 4. Qualitative categorization of 10 environmental variable coefficients for factors[1] and their relationship to the reported incidence of Rocky Mountain spotted fever in four regions of Georgia, 1961–75

Variable	State region			
	South	*Central*	*Lower north*	*Upper north*
Population density	Low	Low	High	Low
Population	Low	Low	High	Low
Public road mileage	Low	Low	High	Low
Elevation	Low	Intermediate	Intermediate	High
Vegetation	Low	Intermediate	Intermediate	High
Precipitation	Low	Intermediate	Low	High
Public forest land	Low	Low	Low	High
Total farmland	Low	Intermediate	High	Low
Harvested cropland	Low	Intermediate	High	High
Frost-free days	High	Intermediate	Intermediate	Low
Incidence of RMSF (per million)	0.7	3.2	10.1	1.9

[1]See table 5 for unit values of variables.

Discussion

Analysis of 10 environmental variables for all of the counties of Georgia (without regard to RMSF incidence) identified two factors composed of subsets of these variables, which, in turn, resulted in the identification of four clusters of counties that had distinct incidence rates of RMSF. We found that the most important variables of those that comprise factor 1 defined clusters that separated north Georgia from south Georgia, the region of lowest incidence, while the important variables comprising factor 2 did not. On the other hand, the variables comprising factor 2 separated lower north Georgia, the region with the highest RMSF incidence rate, from the other two north Georgia regions, which have different incidence rates.

This analysis confirmed observations of various investigators concerning the relationship between the incidence of RMSF and one or more environmental conditions or changes (*4–13*). Most importantly, the method provided a means of simultaneous analysis of all the environmental variables available to us for study and demonstrated which variables were strongly associated with the occurrence of the disease, which had moderate or only slight association, and which had an inverse relationship to the occurrence of RMSF.

Thus, a low value of a climatic-geographic factor (factor 1) was associated with the low incidence rates of RMSF, and a high value of that factor was, in part, associated with high incidence rates. Further, within the high-value climatic-geographic region, the highest value of climatic and human-associated changes (factor 2) was re-

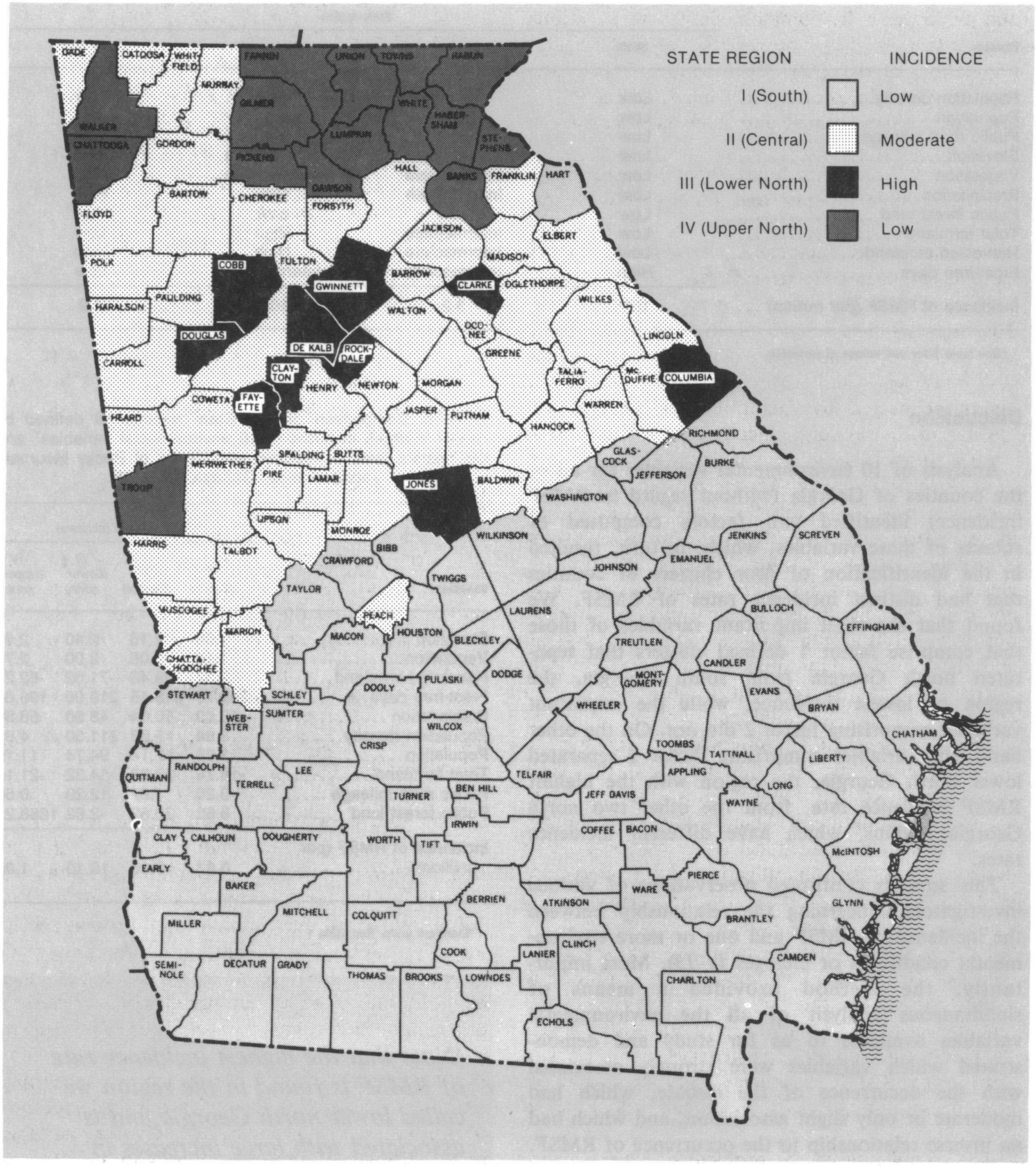
Table 5. Comparison of four State regions as defined by cluster analysis in terms of 10 environmental variables[1] and the relative rates of reported occurrence of Rocky Mountain spotted fever, Georgia, 1961–75

Variables	State regions (clusters)			
	I (South)	*II (Central)*	*III (Lower north)*	*IV (Upper north)*
Elevation	1.05	2.16	2.40	2.80
Vegetation	1.13	2.06	2.00	2.73
Harvested cropland	9.32	-39.48	-71.52	-62.28
Frost-free days	248.70	218.45	219.00	196.80
Precipitation	48.60	50.04	48.50	58.80
Population density	3.64	13.92	211.50	4.69
Population	3.68	17.14	94.74	11.19
Total farmland	-18.74	-33.68	-54.32	-21.16
Public road mileage	-0.26	1.87	12.29	0.50
Public forest land	8.62	30.82	-2.62	1668.22
Incidence of RMSF (per million)	0.67	3.16	10.10	1.93

[1]Standard units. See table 1

'Note that the highest incidence rate of RMSF is found in the region we called lower north Georgia and is associated with large increases in population density, total population, and miles driven on public roads combined with large decreases of farm and cropland . . . '

Figure 3. County clusters and Rocky Mountain spotted fever incidence rates based on factor analysis of 10 social-environmental variables, Georgia, 1961–75.



lated to the highest incidence rate of RMSF, and the lower value was related to a lower incidence rate.

The importance of the climatic-geographic factor (factor 1) suggests that north-central Georgia is ideally suited either to the requirements of the tick vector, *D. variabilis*, or to those of the small wild animal hosts, or both. Since appropriate small wild mammal hosts are found in abundance throughout the entire range of distribution of the tick vector, one might more reasonably conclude that north-central Georgia has climatic-geographic conditions such as humidity and optimal winter temperatures that are ideally suited to the tick vector (*30–31*). Focal areas of RMSF in Massachusetts, New York, and Ohio have in common similar mean winter temperatures slightly above 0° C. as well as large populations at risk (*12*). Mean winter temperatures in south Georgia, on the other hand, at 7°–12° C., are higher than optimal and may have an adverse effect on the tick (*32*).

Factor 2, which includes those variables that directly involve humans and human activity, did not correlate with the incidence of RMSF in the same manner as factor 1. The most important variable of factor 2, as reflected by the largest coefficient, was the increase in population density. This suggests that suburbanization and the associated increase in population density had the strongest influence upon disease occurrence within the region delineated by factor 1, that region most ideally suited physiographically to the tick vector.

This study lacked quantitative data on the prevalence of *D. variabilis*, the most common tick vector of RMSF in the Southeast (*3,14,33*). An investigation was conducted subsequently in Rockdale County, in our lower north Georgia cluster. It was found that *D. variabilis* ticks were not randomly distributed within small study areas, but occurred in aggregates which shifted with time, and that the infection rates were not statistically different in the several study sites (*34*). On a county-wide basis it would appear that the distribution of *D. variabilis* ticks could be considered to be uniform within the habitat type that was characteristic of the county. However, such data for the 159 counties of Georgia are not available. The results of our statistical study can be used to design a prospective investigation of the interaction between the vector ticks and humans in the counties with different attack rates. Further detailed vector information, including relative abundance of *D. variabilis*, competition from other tick species, infection rate of *D. variabilis*, relative abundance of *D. variabilis* infected with various nonpathogenic species of rickettsiae compared with those with RMSF rickettsiae, and frequency of human exposure to ticks, is necessary for such a study.

The complexity of the problem of human exposure to ticks, however, is exemplified by a previous failure to correlate the occurrence of RMSF with the percentage of spotted fever group-positive ticks that were collected from three major geographic areas (*13*). In that report, more RMSF cases occurred in areas that had the lowest percentage of infected ticks, rather than in those with the highest. In Georgia, RMSF has occurred in counties where *D. variabilis* has not been reported, and vice versa (*14*).

'Since the most important variables predisposing to RMSF, namely, climatic-geographic and population density, are not amenable to direct intervention, the most effective preventive measures will remain those taken to avoid tick exposure, such as sufficient protective clothing and proper use of insect repellent.'

Despite possible variation in routinely collected notifiable disease reports, such as more accurate diagnosis and reporting in urban versus rural areas, routinely reported data were found to be predictive of RMSF if the method described in this study is used. Such analyses could be updated to reflect changes in the relevant variables and could be tested as a means to forecast the development of new high-risk areas of RMSF in the State of Georgia. Of course, a prospective analysis of this hypothesis, preferably in other endemic areas, would be necessary to confirm the value of this model in disease prevention.

Since the most important variables predisposing to RMSF, namely, climatic-geographic and population density, are not amenable to direct intervention, the most effective preventive measures will remain those taken to avoid tick exposure, such as sufficient protective clothing and proper use of insect repellent. Public education programs could be effective in areas of greatest risk. More generally, this method might be tested with a variety of other diseases or environmental health problems (for example, certain chronic diseases with unexplained geographic restriction) in complex, multifactorial settings to clarify our understanding of the relative importance of individual variables in the ecology of those conditions in an effort to prevent associated morbidity and mortality.

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