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Intentional Use of Biological and Chemical Agents: Risks and Recommendations

The terrorist acts of 11 September 2001 in the United States have generated a sense of vulnerability that is now being enhanced by the widespread concern of bioterrorist attacks. The discovery of several cases of anthrax in the United States, and additional malicious attempts to spread the bacteria by mail have made this threat very real. This is an opportunity for countries to detect, investigate and respond to the occurrence of potentially epidemic diseases.

Background

Putting aside the use of chemical weapons in war situations around the world since the beginning of the 20th century, only three incidents involving biological or chemical attacks have been documented in the last 16 years. The first one was a deliberate salmonella poisoning in Oregon (United States) in 1984, which resulted in thousands of sick people but no death. The other two involved the use of sarin gas in Japan in 1994 and 1995, and resulted in fewer than 20 casualties.[1] While there have not been large-scale terrorist attacks with biological agents in the past, the recent events have highlighted the need for local public health surveillance systems to be ready to identify, confirm and intervene in acute communicable disease outbreaks. This need is enhanced by dramatic increases in the volume and speed of travel and commerce that further complicates infection control efforts by creating new scenarios for the international spread of infectious diseases. In effect, any local outbreak is considered a threat to all nations. Also, advances in biotechnology increase concern for bioterrorism relating to the possible misuse of genetic research for the development of more potent biological weapons and the spread of new infectious diseases.

However, as public awareness of the threat of chemical and biological terrorism grows, it is important to consider that the actual risk of these forms of terrorism remains small. The reason this risk remains low is the inherent technical limitations involved in acquiring, producing and turning chemical and biological agents into viable weapons. Firstly, chemical and biological agents are difficult to come by. Their acquisition and transport are often complicated and require special equipment. Biological agents, because they are living organisms, require certain handling conditions to survive and be effective agents of disease. Security procedures to curtail access to these agents differ from country to country. Although some strains of dangerous microbes such as *Bacillus anthracis (anthrax)* can be found in natural sources (infected cattle, sheep and camels), it would take great effort to weaponize this agent.

Secondly, there are extreme obstacles to disseminating biological and chemical agents to specific targets. Biological agents must be kept alive and potent and both types of agents must be delivered in quantities sufficient to cause illness. Large quantities of agents would be needed to effectively contaminate drinking water or food and cause disease in many people. Large scale effects might be more efficiently achieved if the agent was delivered in the form of water or aerosol cloud that would then be inhaled by its victims. However, many variables, such as the equipment used and weather conditions could effect the outcome of such a strategy.[2]

For all the above-mentioned limitations, the risk of biological and chemical terrorism remains low. However, the public needs to be educated about the possibilities of this type of warfare, and public health systems must be prepared to identify and contain such outbreaks. Some situations have been defined by the United States military as "epidemiological clues" for the intentional use of biological agents, which when seen together can help in determining if further investigation is needed. These include: more severe disease than expected for a given pathogen, as well as unusual routes of exposure, such as a preponderance of inhalational disease; a disease that is unusual for a given geographic area, that is found outside the normal transmission season, or that is impossible to transmit naturally in the absence of the normal vector for transmission; and unusual strains or variants of organisms or antimicrobial resistance patterns disparate from those circulating.[3]

Biological and chemical agents

Several microorganisms have been identified as serious enough threats to warrant preparation by the public health system: *B. anthracis* (anthrax), variola virus (smallpox), *Yersinia pestis* (plague), *Clostridium botulinum* (botulism), *Fran-*

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ciscella tularensis (tularemia) and hemorrhagic fever viruses.[4] Chemical agents include mustard and sarin gas.

There has not been any case of smallpox in the Americas since its eradication from the Region in 1971. Some of the diseases mentioned above occur in endemic form in the Region. The natural form of anthrax is relatively frequent in South America and is present in cattle in the United States and Canada. Countries that report plague in the Region include Brazil, Peru, Bolivia and the United States.[5] It is known that Tularemia occurs throughout much of North America (every state in the United States has reported human cases although most cases occur in the South Central and Western states.)[6] Finally, the botulinum toxin can be found worldwide.[7]

Points regarding anthrax[8]

Anthrax does not spread from person to person, but can be made into a powder that can, with relative ease, be made into a form that is easily dispersed. It requires that cases be detected as early and as quickly as possible; emergency room personnel must be trained and alert. The public health system must be strengthened and include knowledgeable staff in infectious diseases, in more or less the same way as required for emerging infectious diseases. A network of laboratories is necessary to identify the infectious agent.

Currently, a good anthrax vaccine is not available. The United States of America has stepped up its research on new anthrax vaccines. Now the best response to exposure is prophylaxis with antibiotics for 60 days after exposure. Anthrax is greatly sensitive to a wide array of antibiotics other than ciprofloxacine. Penicillin and doxycycline are recommended.

Points regarding smallpox[8]

Currently, large populations have no immunity to smallpox; the number of individuals susceptible to the infection is larger than ever, given that immunization stopped over a quarter of a century ago, and very few people may have natural immunity. Although smallpox is more difficult to release, if it were released, its hazard potential would be much higher than that of anthrax. Smallpox would become an immediate international problem. Countries which in the past had the capacity to produce smallpox vaccine can no longer do so, and regaining that capacity would require training and revision of production procedures. An international initiative is necessary to re-establish capacity for smallpox vaccine production if it were needed.

The United States has decided to restart the production of smallpox vaccine. The strain to be used is the traditional one, i.e., the New York Board of Health strain. Two or maybe three sites will produce the vaccine. See Box 1 for sources of information on the other agents mentioned above.

The Pan American Health Organization (PAHO)'s response

Following the terrorist acts of 11 September, PAHO received numerous inquiries from the Organization's Member States about the response that countries should prepare for in case additional events of this nature should occur. In response to these concerns, PAHO's Director, Dr. George A.O. Alleyne, convened a consultation meeting of experts on bioterrorism from the Region of the Americas. The purpose of the consultation was to examine current and future challenges and opportunities facing PAHO and to provide recommendations for the Organization's technical cooperation in regard to prevention, control and response to threats or acts of bioterrorism. This meeting took place at PAHO Headquarters on 24 October 2001. The themes discussed during the meeting generated the following conclusions and recommendations.[8]

Conclusions

- Preparedness for the threat of natural and man-made disasters and the surveillance of emerging and reemerging infectious diseases provides some guidelines on how to deal with bioterrorism. Part of the role of the public health system of any country is to be prepared for mass casualties of any cause and kind. In particular, containment of the source of contamination should be managed by the disaster preparedness structure in each country.
- It is the health sector at the local level (hospitals, emergency personnel) that must deal with consequences of a bioterrorist attack. Indeed, it is possible that biological damages will not be apparent until the affected population seeks emergency room services due to sickness. First respondents in these cases will be hospitals, especially emergency health care personnel. Therefore, the health sector must be included early in the planning for these situations. Although the hospital capacity may be a concern in a bioterrorism situation, emergency plans in some countries include procedures to make beds available during emergencies.
- Epidemics, of known or unknown etiology, often induce panic and cause damage beyond the disease itself. In 1994, an outbreak of plague in India led to hundreds of thousands of people fleeing the city of Surat. Other consequences included embargoed flights to and from India, and restrictions on importation of Indian goods.[9] Therefore, public information is a key part of the response to emergency situations and governments must provide complete and accurate information to prevent panic and maintain viable and effective public health surveillance networks.

Recommendations

Two sets of recommendations were issued by the PAHO consultation group. The first addressed national preparedness and the second, PAHO's technical cooperation.

Regarding national preparedness, recommendations deal with general preparedness, public health surveillance, and laboratory capacity:

General

- The threat of bioterrorism should be included in every country's plan and structure to deal with disasters. These plans should be multisectoral and supported by training of all sectors and desktop simulation exercises.
- These plans should cover detection, diagnosis and response.
- Plans should include an inventory of the human and physical resources available.
- Countries should be prepared to provide up-to-date and

Box 1: Selected Sources of Information on Biological and Chemical Agents

Health aspects of biological and chemical weapons (World Health Organization):http://www.who.int/emc/pdfs/BIOWEAPONS_FULL_TEXT2.pdf

The Public Health Response to Biological and Chemical Terrorism (CDC): http://www.bt.cdc.gov

Guidelines for the Anthrax, Botulism, Smallpox and Plague: Hopkins Antibiotic Guide (Johns Hopkins University Center for Civilian Bio-defense studies): http://www.hopkins-biodefense.org

The Global electronic reporting system for outbreaks of emerging infectious diseases and toxins: http://www.promedmail.org

Assessing the Health Consequences of Major Chemical Accidents: Epidemiological Approaches (WHO): http://www.who.int/disasters/tg.cfm?doctypeID=19

INTOX Databank on toxic agent (International Programme on Chemical Safety (IPCS): http://www.who.int/pcs.index.htm

Responding to the deliberate use of biological agents and chemicals as weapons (World Health Organization): http://www.who.int/emc/deliberate_epi.html

Frequently-asked questions on bioterrorism and chemical terrorism (World Health Organization): http://www.who.int/emc/questions.htm

accurate information relevant to the protection of public health.
- Countries should share information on results of epidemiological investigations and cooperate with each other in response to events.
- Countries should have expert commissions on bioterrorism by creating new ones or preferably by using and expanding existing disaster preparedness bodies.

Surveillance
- Countries should take steps to enhance their ability to detect, identify, investigate and respond rapidly to reports of emerging infectious diseases. This may include the establishment of rapid response teams.
- Health care providers should receive training in diagnosis and reporting of clinical presentations consistent with man made epidemics, beginning with emergency room personnel, followed by primary health care staff.
- There should be specific written procedures for the safe handling and transportation of infectious disease materials.
- Treatment guidelines should be available to address the biological agents discussed.

Laboratory capacity
- Laboratory networks should be improved for the diagnosis of potential agents used in bioterrorism.
- Laboratory biosecurity should be strengthened to prevent theft, misuse, contamination or improper handling of these agents.
- There should be national and international quality control of laboratory diagnosis.
- Laboratory personnel should be trained in the recognition of findings suggestive of bioterrorism agents.
- Transfer of infectious samples among laboratories should be done according to established guidelines and confirmed by sending and receiving institutions.

PAHO's technical cooperation

PAHO should:
- Provide authoritative, current information to countries on events related to bioterrorism, which could be used in the preparation of national plans.
- Make recommendations for prophylaxis and treatment of anthrax.
- Together with countries of the Region, explore the potential for production of smallpox vaccine, to include update of good manufacturing practices (GMP) for production.
- Support countries in the development of national plans to address bioterrorism.
- Provide training to countries in the surveillance, laboratory and information aspects related to the response to agents used in bioterrorism.
- Identify reference laboratories for confirmation, training, and provision of reagents.
- Promote the development of rapid diagnostic tests and availability of diagnostic reagents for anthrax and other potential agents of bioterrorism.
- Support quality control and proficiency testing in the laboratory for diagnosis of agents of bioterrorism, including the provision of an inventory of reagents available for this purpose.
- Support cooperation among countries, including through subregional networks.
- Coordinate rapid response to support countries to deal with bioterrorism.

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Source: Prepared by Ms. Anne Roca, Mr. Byron Crape, Ms. Genevieve Chase, Dr. Enrique Loyola and Dr. Carlos Castillo-Salgado of PAHO's Special Program for Health Analysis (SHA).

SIGEpi: Geographic Information System in Epidemiology and Public Health

Introduction

Since 1995, in response to the health services needs of the countries of the Americas, the Special Program for Health Analysis (SHA) of the Pan American Health Organization (PAHO) developed a technical cooperation project, the purpose of which is the dissemination and use of Geographic Information Systems (GIS) as a tool for analysis and problem-solving in epidemiology and public health[1] (SIG-SP for its Spanish name).

Generating a series of activities, this project promotes development of low-cost computer systems, among them the software package SIGEpi. The SIGEpi package offers simplified tools and interfaces to efficiently carry out biostatistical and geographical analysis to support decision-making in public health.

Background information is presented here on the development of SIGEpi, its characteristics and general functions, as well as an example of how its analytical tools can be used. In this article, SIGEpi is applied to identify populations exposed to environmental risks in Mexico.

Background

Resulting from meetings, seminars, consultation workshops and requests made directly to the SIG-SP Project, some of the most common problems in the use of GIS in public health were defined as: high costs of commercial GIS software packages, making them inaccessible to the majority of users; insufficiency of epidemiological and public health analysis tools in GIS; and lack of integration between statistical and epidemiological programs and GIS.

To address such limitations, development *components*[a] from commercial programs were taken advantage of, particularly those handling cartographic data which allow the user to create products that can be distributed at a low cost and respond to the specifications and requirements proposed in the Project. With this consideration, SIGEpi was built based on ESRI's[2] MapObjects™.

SIGEpi's Beta version is currently used as an analytical tool for the surveillance and control of malaria in Brazil, and in a project to prevent the reintroduction of DDT for malaria control in Mexico and Central America.

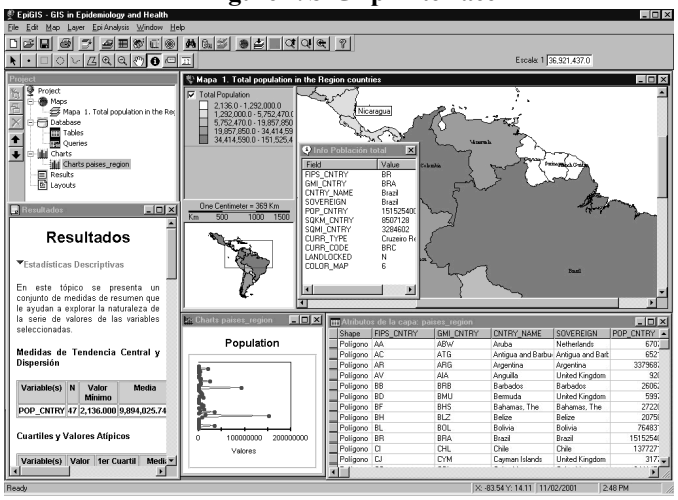
Principal characteristics of SIGEpi

Developed for personal computers (PC) on the Windows platform, SIGEpi was designed following the conceptual elements and general systemic framework of the PAHO GIS[3] proposal.

SIGEpi's graphic interface permits the management of multiple types of programs (from this point on they will be referred to as documents), each in independent windows.

[a] *Component*: a block of programs that brings together a set of discrete functions, operations, logic and user interface that can be used in the development of other programs.

Figure 1: SIGEpi Interface



Typical documents consist of: Projects, Maps, Tables, Graphs, Results, and Presentations; each with its own functions, menus, buttons, and tools (see Figure 1).

Project controls all other documents and forms of data presentation, and guarantees that the current work session can be recovered in future sessions in the same state as was saved.

Data presentation and visualization are rendered through maps, tables and graphs. A dynamic link is maintained between them, allowing for simultaneous queries among the table, map, and graph registries. The Map document is the central document in a GIS, allowing the incorporation, manipulation, classification and visualization of cartographic data. The Tables document enables the presentation and handling of the databases' cartographic layers and attributes, while the Graph document shows alternate representations of the map layers attribute data.

The "Results" section, visualizes in HTML format the results from processing and statistical analysis of data, producing data that can be managed in a word processor program or published on the Internet. The "Presentations" section prepares documents for high quality printing.

Functionality of SIGEpi

From a data management standpoint, SIGEpi follows an open approach and does not require the establishment of an *a priori* structure. This approach offers greater versatility in a framework where the user decides on the type of application and data necessary for its development, allowing the user to take advantage of data existing in other information systems.

Management of the digital maps is based on the vector model. It has the capacity to read and process files in *Shapefile* and *ArcInfo coverage* formats from ESRI; other formats include *Vector Product Format* (VPF) (.pft, .lat, .aft, .tft); CAD (.dwg, .dxf) and EpiMap (.bnd).

The SIGEpi system also can integrate different image formats and display them as a background image for a map. In addition, SIGEpi's database management system handles MS Access'97 (.mdb) databases as the native format, and allows for the importing/exporting of data tables from other popular formats such as Excel, Dbase, Btrieve, EpiInfo, ASCII delimited text, etc. Database tables can be linked through an index to cartographic bases and overlaid on a map. Other operations and calculations also can be carried out for epidemiological analysis.

The design and selection of analytical procedures in SIGEpi are the product of a systematic and shared effort with the project's collaborating groups, and other professionals and experts in public health. Following are the principal processing and analytical functions, according to their areas of application, offered by SIGEpi.

a. Basic functions and spatial data processing (geo-processing)

Data management and processing functions are: integration of attributes from data tables with digital cartographic bases (layers of spatial data), for visualization on a map through the superposition of multiple data layers; selection and querying of spatial data to generate new layers based on attributes and spatial operations between layers; geo-referencing or plotting points on a map from data tables with x, y coordinates; geo-processing operations such as the creation of catchment areas (*"buffers"*) to delineate areas of impact or influence, and production of radial schemes (*spider-diagrams*) to measure linear distances between origin and destination.

Another essential function of SIGEpi is the creation of thematic maps, such as unique value or dot-density maps, bar and pie graphs, and intervals or ranges calculated with different classification methods.

b. Quantitative methods in Epidemiology

The functions include measures for quantitative analysis in epidemiology, which are particularly useful in exploratory data analysis. Among them are: descriptive statistics to calculate the set of measures of central tendency and scatter and prepare frequency distributions; correlation analysis; and both simple and multiple linear regression. Some functions for the calculation of rates, ratios, and proportions are included, as well as adjustment using direct and indirect methods[4] and spatial smoothing[5].

c. Useful methods for Public Health Practice

Some methods useful in analysis and decision-making processes in Public Health have been incorporated in SIGEpi. These include: identification of critical and priority areas; construction of a composite health index —such as basic unmet health needs or poverty - or identification and detection of spatial and time-space clusters[6]; measurement of the association between environmental exposure factors and health events for case-control or cohort epidemiological studies[7]; and evaluation methods for access to health services (based on the radial schemes technique), such as a simple measure of accessibility using linear origin-destination distances. An example of the use of SIGEpi in the area of environmental health is presented below.

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Source: Prepared by Eng. Ramon Martinez, Mr. Manuel Vidaurre, Geog. Patricia Najera, Dr. Enrique Loyola, Dr. Carlos Castillo-Salgado and Mr. Charles Eisner from PAHO's Special Program for Health Analysis (SHA).

Use of SIGEpi for the Identification of Localities Vulnerable to Environmental Risks in Mexico

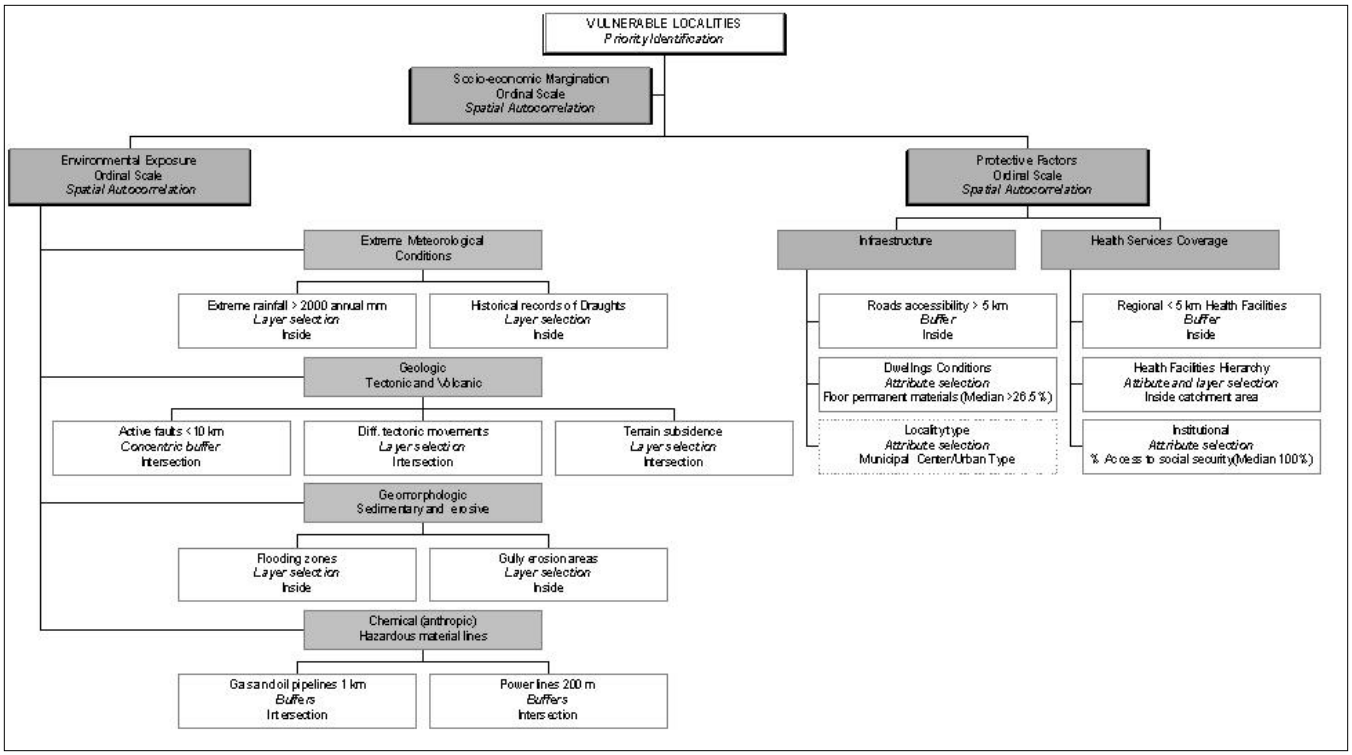
Problem under study

In various areas of Central Mexico, in the state of Querétaro in particular, a group of localities with high levels of marginalization[1] can be found. They are potentially vulnerable to the influence of extreme environmental risks or events derived from land dynamics of the region. These risks fall into several categories, depending on their origin[2]: 1) Hydrometeorological risks: disasters derived from severe droughts or high levels of rainfall; 2) Geological risks: proximity to active fault lines, with regard to differential tectonic movements, or terrain subsidence; 3) Geomorphologic risks: Dynamics of different relief types, some prone to erosion and in others, flooding and sedimentation; 4) Chemical risks, resulting from human activity: proximity to electric lines or pipelines transferring hazardous materials, such as gas or oil.

The vulnerability of a locality to environmental risks is understood as the occurrence of emergencies or demands that exceed the capacity of the health sector to respond.[3] Lack of resources or distance to infrastructure and services increase the problem. Indeed, a large number of communities do not have health care centers in close proximity, are far from principal transportation routes, and lack sufficient resources in case of environmental disaster, the latter due to the precarious and temporary nature of the materials used to build their dwellings.

In order to enhance the measurement of vulnerability, a five-level socioeconomic *"marginalization"* index officially used in Mexico, was adopted as a synthetic measure. This index was constructed using the method of principal compo-

Figure 1: Conceptual and Operational Framework for the Identification of Vulnerable Localities: Application of Consultation, Selection and Spatial Analysis Tools in SIGEpi



nents, and is used to differentiate states, municipalities and localities according to the global impact of deficiencies in access to elementary education, conditions and size of the dwellings, population distribution and an income insufficient to acquire the basic basket of food[4].

The magnitude and distribution of vulnerability in central Mexico is partially known in different sectors of the public administration. However, given the diversity of information sources and the lack of adequate methodological tools, it is difficult to prepare a comprehensive diagnosis including environmental, social and economic data. The data associated with the health system's response capacity are particularly difficult to include in the diagnosis.

As a first approach to the problem of identifying, quantifying and locating areas exposed to environmental risks in the state of Querétaro, an application was developed using geo-processing and statistical/spatial analysis tools available in SIGEpi. Production took into account marginalization, access to protective factors, and the presence of environmental risks, and was carried out under the operational model shown in Figure 1. It is important to point out that this framework was the basis for the construction of criteria, classification of variables and analysis of its relations.

Methods

1. Sources of Information

Various layers of digital cartographic information and attributes were compiled from different sources. They were incorporated into the project by their geometric characteristics: *point* files (localities[5], with or without health services); *lines* (roads, pipelines[6]) and *polygons* (municipalities[7], layers of environmental risks[8,9]). Environmental risks were defined in relation to the criteria established by the agencies that provided the information.

Base maps were prepared previously using the Universal Transverse Mercator projection (UTM), zone 14Q, where the state of Querétaro is located, in order to carry out the measurements of areas and distances with greater precision[b]. To simplify geo-processing and structuring of the attribute table and data analysis, two separate layers were formed using information on localities in each state: those considered as headquarters for public health services and the remaining localities without public health services. There are a total of 2,112 localities of different sizes in the 18 municipalities of the State of Querétaro, but 28.3% are communities with two dwellings or less, for which no population nor socioeconomic information exists. For purposes of this study, these were eliminated from the analysis.

2. SIGEpi tools used for processing and analysis

Creation of point layers

Through this procedure, the geo-referencing of the clinics and hospitals not belonging to the Ministry of Health of the State of Querétaro[10] (SESEQ) was carried out, based on the geographical coordinates of the headquarter localities[11,12,13]. These health service units were added to the services of the SESEQ in a single layer in order to cover all public health services available in the state of Querétaro.

[b] The projection module has not been incorporated in the Beta version of SIGEpi.

Creation of areas of influence

Influence areas were set up to identify catchment area reach of two types of phenomena: 1) impact areas of environmental risks, such as fault lines, or those of electric lines (200 m) or gas/oil pipelines (one km), and 2) an area 5 km from both health centers and transportation routes available all year, according to PAHO's definition.[14]

Access to services (radial schemes)

With this tool, the shortest linear distance was drawn between a central point (health centers), and satellite or peripheral localities.

Selection by attributes and by layers

These techniques were applied to place localities in relation to environmental risks, or influenced by the protection of services and infrastructure. Through this process and geoprocessing, environmental risk zones were geographically delimited.

Criteria used to select localities with protective factors included the following conditions[c]: percentage of the population with social security (median value was 0%); dwellings with some floor covering (the median value was 26.5%) and level of urbanization (more than 10,000 inhabitants). Also, they had to fulfill some categorical value, such as whether they were a municipal government center or not.

In the same way, a selection by layers identified localities within areas of influence or risk, or localities intersecting areas near electric lines or fuel ducts. Once identified, dichotomous values (0,1) were assigned to those localities meeting the conditions established within the operational framework.

Frequency distribution and exploratory data analysis

Exploratory data analysis was carried out for the variables under analysis. Median values were calculated in order to establish cut-off values for the selection of critical localities.

Identification of critical areas (critical localities)

Localities were classified depending on an expected (cut-off) value. The dichotomous score assigned to the communities was added in order to generate an ordinal scale, ranging from 0 to 4, depending on the number of exposure factors.

A similar process was followed for protective factors, with criteria such as the proportion of dwellings built with permanent materials, proximity to roads, or social security coverage; other criteria included the availability of health services located within 5 km and classified by levels of care: hospitals, clinics, and health centers.

Subsequently, we selected localities of greater vulnerability that fulfilled all conditions at the same time, i.e., exposure to risk factors, lowest level of protective factors and greatest marginalization (based on the original official classification).

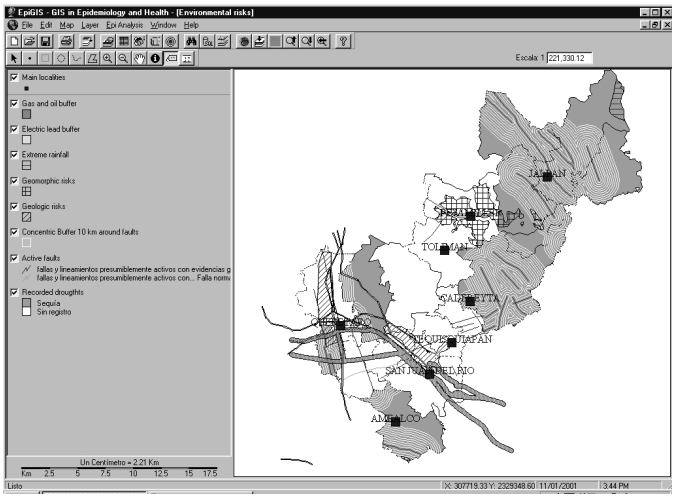
Spatial autocorrelation

This method is used to determine if an indicator's value shows a tendency to form geographical clusters or if its distribution is random. Moran's global autocorrelation index (I) is calculated for a global test to determine the existence of significant clusters in the distribution of data without indicating where it is located.[15] With the local test, it is possible to identify the location of the clusters.

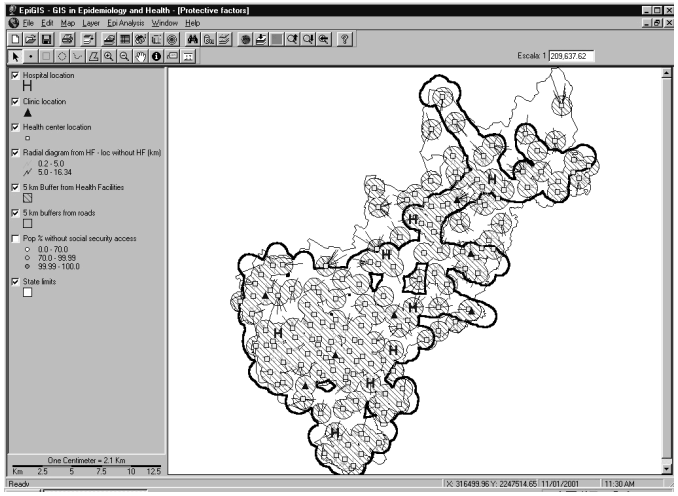
For this particular study, Moran's global I was calculated for the following variables: exposure to environmental factors, access to protective factors, and marginalization, using a radius of 5 km as criterion for vicinity.

[c] The cutting points correspond to the median values for each variable.

Map 1: Environmental Risk Zones in the State of Queretaro, Mexico



Map 2: Protective factors and Relation of localities with health services, Queretaro, Mexico



Results

The limit, extent, and overlap of environmental risk areas are shown in Map 1. Nine municipalities were found with historical records of drought, the majority located in the Sierra Gorda (Northeast of the state). Small areas with reports of extreme rains and floods were found in the Southern and Northeastern end of the state. Active faults concentrations also were detected in the area of the Sierra Gorda (NE) and in the Neovolcanic Axis range located in the Southwestern extreme of the State. Geological risk zones (areas of subsidence

and tectonic movements) also were found to the Southwest of the state. Furthermore, areas of environmental changes due to human activity were identified, such as areas close to high-voltage lines or pipelines of hazardous materials (gas and oil) in the zone known as the industrial corridor of San Juan del Río – Querétaro.

In contrast, the distribution of protective factors, as seen in Map 2, includes both areas with roads and health care units, classified by health care capacity (hospitals, clinics and health care centers). These catchment areas are delineated within a distance of 5 km, equivalent to a hour-long walk on flat terrain. In addition, parts of the state not covered by this infrastructure are shown. The distances between localities and health centers greater than 5km are highlighted by the radial schemes.

Among the 1,447 communities with socioeconomic information, 172 have health units with different levels of capacity - hospitals, clinics, and health centers - and 1,275 do not, the latter having an average population of 254 inhabitants (range from 5 to 3,392 inhabitants).

Of the 1,275 localities under study (without health care units), we find that 1,110 (91.5%) are exposed to at least one risk factor in the surrounding environment, either natural or human-made. In only 7 of the analyzed localities, do all four environmental risk elements appear together (Table 1).

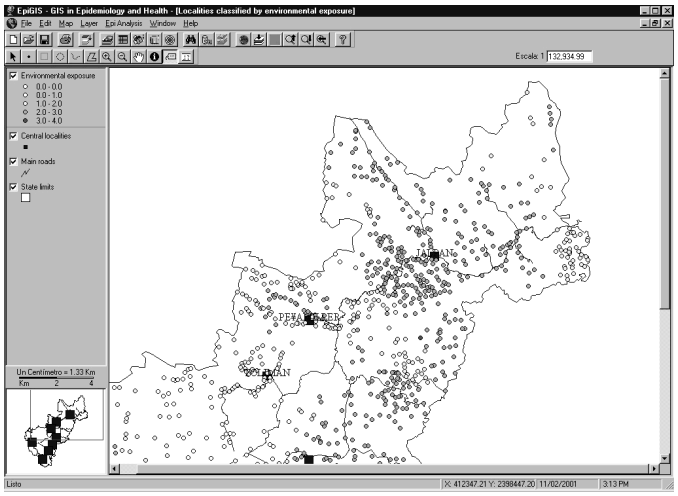
With regard to protective factors, 849 localities representing 42.7% of those under observation register spatial concurrence in at least four of the seven existing levels. It is notable that only 47 communities (3.7%) have all protective factors.

Finally, we find that 626 localities (49.1% of the total without health services) are classified as communities of high and very high marginalization, defined as values of 4 and 5

Table 1: Frequency Distribution for a Selection of Variables

Environmental Exposure	Absolute Frequency	Relative Frequency (%)	Cumulated Frequency (%)
0.0	121	9.5	9.5
1.0	506	39.7	49.2
2.0	610	47.8	97.0
3.0	31	2.4	99.5
4.0	7	0.6	100.0
Protective Factors	**Absolute Frequency**	**Relative Frequency (%)**	**Cumulated Frequency (%)**
0.0	3	0.2	0.2
1.0	71	5.6	5.8
2.0	74	5.8	11.6
3.0	233	18.3	29.9
4.0	350	27.5	57.3
5.0	460	36.1	93.4
6.0	37	2.9	96.3
7.0	47	3.7	100.0
Marginalization Values	**Absolute Frequency**	**Relative Frequency (%)**	**Cumulated Frequency (%)**
1.0	44	3.5	3.5
2.0	76	5.9	9.4
3.0	231	18.1	27.5
4.0	298	23.4	50.9
5.0	626	49.1	100.0

Map 3: Localities classified by their Exposure to Environmental Factors, Queretaro, Mexico



according to the official categories use by the Mexican agencies CONAPO-PROGRESA.

The map classifying localities by environmental exposure level, identified several areas in the state where various risk factors coincided (map 3). Areas of interest include the industrial corridor of San Juan del Río Querétaro (to the Southwest of the state), with four factors; Amealco (to the South) with three coincidental risk factors; vicinity of Jalpan in the Sierra Gorda (Northeast of the state) with combinations of two environmental factors; and Peñamiller and Cadereyta, in the center of the state.

Additional thematic maps were constructed to analyze the regional distribution of localities under certain conditions of protection and marginalization (not included).

Based on a classification of protective factors with an ordinal scale, it was possible to recognize groups of localities with high values as determined by the weight of the classification of health care units. The highest values appear to the South Southwest of the state, coinciding again with the industrial corridor of San Juan del Río – Querétaro. The following lower values are found around the other central localities (government headquarter and/or urban).

In addition, the analysis of the regional distribution of localities with high marginalization showed an important concentration in the Northeastern area of the State—corresponding to the Sierra Gorda – however, other concentrations are found toward the periphery, in areas far from the principal lines of communication.

The statistical significance of Moran's I for risk exposure is showing that its distribution is not random and that the exposure values tend to concentrate in certain places of the state. It also shows that there exists groups of neighboring localities with similar values of exposure (Table 2), within the 5km limit. The levels of protection and marginalization show a clustering of neighboring communities, similar to the environmental exposure.

As a result of applying criteria analysis to synthesize the three groups of factors, a group of 379 critical localities

Table 2: Global Spatial Correlation Indices for Factors Associated to Vulnerability

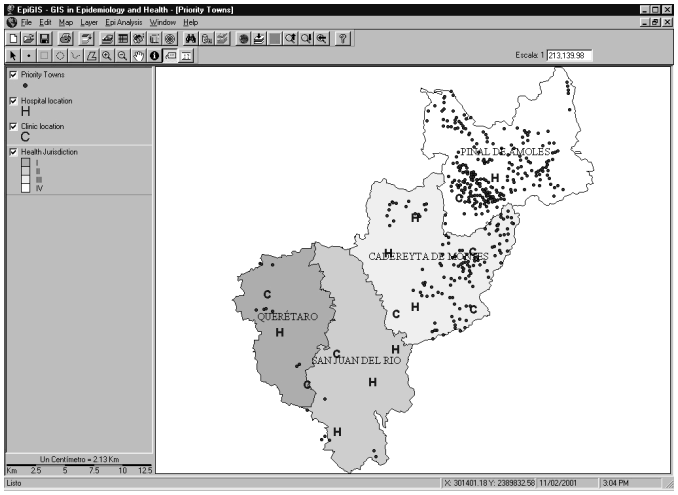
Moran's I (5km)	Calculated Value of I	Expected Value of I	Standard Deviation of I	Z score de I	Significance (p)
Environmental Exposure	0.7154	-0.0008	0.0146	49.1277	0.00000
Protection	0.5556	-0.0008	0.0146	38.1662	0.00000
Marginalization	0.4184	-0.0008	0.0146	28.7524	0.00000

were identified, where 55,083 people (4.4% of the state population) live, under greater environmental exposure, very little protection and high marginalization. Map 4 shows the elevated concentrations of these localities to the Northeast of the state, in the Sierra Gorda zone.

For purposes of estimating population and determining necessary resources to serve the populations in each health jurisdiction, the total of all localities in each administrative unit was calculated. The lowest concentration of critical communities is located in health jurisdiction I (Southeast), with 9 vulnerable localities and 953 inhabitants representing 0.1% of the jurisdiction's population (Table 3). At the other extreme, jurisdiction IV (Northeast or Sierra Gorda), registers 242 vulnerable localities and 33,993 inhabitants (42.2% of the jurisdiction's total population).

In absolute terms, we observe that the jurisdiction with the highest level of development and largest population (I) has a very small vulnerable population. In contrast, the health jurisdiction with the smallest population, fewest resources, and lowest level of development (IV) shows a highest number of vulnerable localities and population.

Map 4: Critical Localities by Jurisdiction, Queretaro, Mexico



The health services response are limited by the availability and specialization of health care facilities. The ratio of vulnerable population per unit of first level care is 50 times higher in Jurisdiction IV that in Jurisdiction I. Also, the number of available care units with high specialization is lower in Jurisdiction IV.

Conclusions

Within a vulnerability analysis framework, tools such as SIGEpi allow the integration of measures and indicators from different sources, and place them in a common space for statistical and geographical analysis. Using this, it is possible to delineate natural hazards in a geographical region, approximate the scale of situations requiring response capacity which exceeds that of the health services and accordingly, evaluate some approaches to mitigate the vulnerability of populations and infrastructures exposed to environmental risks and disasters. This analysis is necessary to support and direct the decision-making process on priorities and interventions. Although not an exhaustive analysis, factors related to risk exposure were weighted according to their potential impact. This allows both the recognition and ability to take advantage of those procedures that determine risk. To this end, traditional univariate and multivariate analytical tools were used, including the value of spatial perspective.

Prospects for SIGEpi

With many issues concerning requirements and needs still facing GIS applications in public health, the solutions presented by SIGEpi, through its analytical tools for epidemiology and public health, open a favorable perspective for this GIS package.

Prior to its launching, SIGEpi, currently in its Beta version, has been tested by various Latin American and Spanish institutions. Their suggestions are being incorporated into the program, and a series of functions still have to be incorporated into the package in the near future. Overall, the design of this SIGEpi has followed a systematic and evolutionary development whereby corrections, suggestions, and observations from internal and external reviewers have been incorporated.

The distribution of SIGEpi will be done by interinstitutional agreements between SHA/PAHO and health/academic institutions interested in its use for diagnosis and evaluation projects, or research in the area of public health and epidemiology. For more information contact Dr. Carlos Castillo-Salgado, Special Program for Health Analysis, PAHO; E-mail sha@paho.org.

Table 3: Distribution of Critical Localities in each Jurisdiction

Jurisdiction	Critical Localities	Vulnerable Population	Total Population by Jurisdiction	Vulnerable Pop./ Total Pop. (%)	# First-level Units	# . Hospital Units	Vulnerable Pob./Unit Level Ratio
I. Querétaro	9	953	706,566	0.1	50	4	19.1
II. San Juan del Río	7	2,579	340,821	0.8	58	4	44.5
III. Cadereyta	121	17,558	122,503	14.3	49	3	358.3
IV. Pinal de Amoles	242	33,993	80,586	42.2	35	1	971.2
State Total	379	55,083	1,250,470	4.4	192	12	286.9

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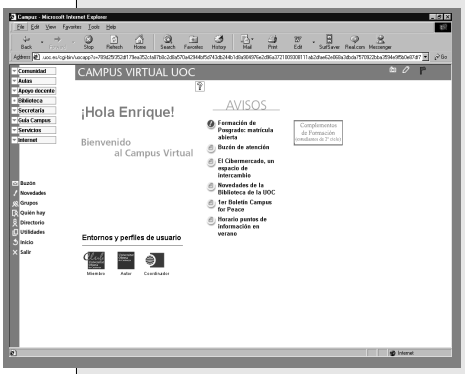
Source: Prepared by Geog. Patricia Najera, Eng. Ramón Mártinez, Mr. Manuel Vidaurre, Dr. Enrique Loyola, Dr. Carlos Castillo-Salgado and Mr. Charles Eisner from PAHO's Special Program for Health Analysis (SHA).

II Internet-based Distance Course on the Bases of Epidemiology and Biostatistics in Spanish

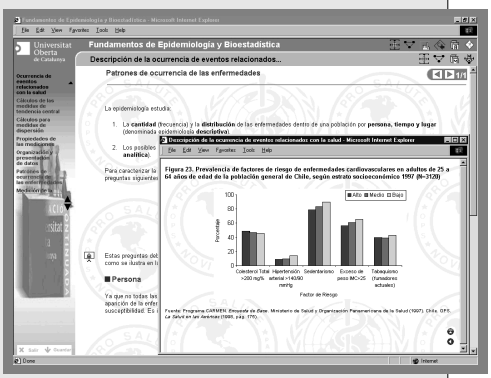
The Special Program for Health Analysis (SHA) of the Pan American Health Organization (PAHO) and the Universidad Abierta de Cataluña (UOC) of Spain, recipient of the best virtual university award, are organizing the **II Distance Learning Course on the Bases of Epidemiology and Biostatistics**, offered **in Spanish** through the Internet starting in July of 2002. This second version has been created as a continuing education program in Epidemiology and Public Health Services. The characteristic of this program is that it is based on the development of professional skills for the practice of epidemiology. Accordingly, the process of learning is oriented to the resolution of real-life problems addressed by professionals in their daily work.



General objectives: It is expected that after completing the course, students will be capable of: 1) recognizing the theoretical and practical bases of Epidemiology and Biostatistics in the health sciences, 2) Using the basic terminology in Epidemiology and in Biostatistics, 3) Formulating the epidemiological and statistical description of scientific information, 4) Posing and solving basic problems of inferential statistics in the area of health, 5) Recognizing and using the measures and main designs used in Epidemiology, 6) Applying the concepts and practices of Epidemiology and Biostatistics to different public health scenarios.

Organization of the Course: The course's thematic units are organized in 7 modules. Two of them are devoted to online learning methods and computational tools, while the rest includes concepts and fundamental methods of epidemiology and basic tools of biostatistics required for the epidemiological analysis of the health status and its determinants. The participants who pass the course will receive an academic certificate with credit value corresponding to 9 virtual units (equivalent to 6 traditional credit hours).

The course has an approximate duration of 6 months, initiating on the 1st of July 2002. There will be participation of international tutors devoted to a maximum of 7-8 students. There will be a limit of 35 students, who will be selected by an internal committee, in accordance with their qualifications, on a first-come first-served basis. The tuition consists of a recovery cost of $1,500 that covers administrative, registration costs and all materials.



Application: Applications should include name, age, address, current position, degree, previous courses, and a recent photograph, in accordance with the application form (available at: http://www.paho.org). Each student should have access to a computer and to the Internet. Applications will be received from this date until 1 May 2002. Admitted students will be informed of their selection in May.

Applications indicating commitment and sources of financing (SHA does not grant fellowships) should be sent to the following address: Special Program for Health Analysis, Pan American Health Organization, 525 23rd Street, NW - Washington, DC 20037 U.S.A., Email: sha@paho.org

Influenza: Basic Epidemiological Aspects for the Development of Vaccines

The Disease

Influenza (the "flu") is one of the most notorious human ailments. First described by Hippocrates in 412 BC, it is one of the oldest and most common human diseases, affecting large portions of the world population in seasonal epidemics each year. While the symptoms of the flu are often mild in nature, the ever-changing influenza virus can lead to deadly pandemics. Surveillance and vaccine preparation - two important activities of influenza control - are therefore indispensable to prevent its potentially deadly effects.

Influenza virus

Influenza viruses are classified as A, B and C. Influenza A and B are the two types that cause epidemic human disease. Influenza A viruses are further categorized into subtypes on the basis of two surface antigens: hemagglutinin (H) and neuraminidase (N). The development of antigenic variants through a process called antigenic drift is the virologic basis for seasonal flu epidemics.

Clinical Signs and Symptoms

Influenza viruses are spread from person-to-person primarily through the coughing and sneezing of infected persons. The incubation period for influenza is 1-4 days, with an average of 2 days. Persons can be infectious starting with the first symptoms through approximately 5 days after illness onset; children can be infectious for a longer period. Uncomplicated influenza illness is characterized by the abrupt onset of constitutional and respiratory signs and symptoms (e.g., fever, myalgia, headache, severe malaise, nonproductive cough, sore throat, and rhinitis). It typically resolves after several days for most persons, although cough and malaise can persist for more than 2 weeks. In some persons, the disease can exacerbate underlying medical conditions (e.g., pulmonary or cardiac disease), lead to secondary bacterial pneumonia or primary influenza viral pneumonia, or occur as part of a co-infection with other viral or bacterial pathogens.

Epidemiology of Influenza

Seasonality

In the temperate and cold climates, the flu usually causes winter epidemics: December-March in the Northern Hemisphere; June-September in the Southern Hemisphere. In tropical and subtropical areas, influenza epidemics can occur either twice a year or even throughout the year. As mentioned before, these seasonal epidemics occur due to antigenic drift.

More rarely, major antigenic changes occur in the viruses that can cause pandemics (worldwide outbreaks of an influenza virus subtype to which the human population has no protection). The most severe infectious disease disaster of the 20th century was the "Spanish" influenza pandemic of 1918, which killed more than 40 million persons worldwide. Other more recent pandemics were the 1957 "Asian" flu and the 1968 ""Hong-Kong" flu.

Surveillance

Respiratory illness caused by influenza is difficult to distinguish from illness caused by other respiratory pathogens on the basis of symptoms alone. The reported sensitivity and specificity of clinical definitions for influenza-like illness that include fever and cough have ranged from 63% to 78% and 55% to 71%, respectively, compared with viral culture. Sensitivity and predictive value of clinical definitions can vary, depending on the degree of cocirculation of other respiratory pathogens and the level of influenza activity. For these reasons and because the influenza strains identified during one season are useful to help define the influenza strains to be recommended for the next season, **virologic surveillance** is the most important element of influenza surveillance. The recommended case definition of influenza is presented in Box 1.

Groups at highest risk

Although influenza viruses cause disease among all age groups, severe complications and death are highest among the elderly and among persons of any age suffering from chronic respiratory and cardiac conditions. The main tool for prevention of influenza is the yearly vaccination of persons at high risk with the inactivated influenza vaccine. According to the United States Centers for Disease Control and Prevention (CDC)'s Advisory Committee on Immunization Practices (ACIP), the primary target groups recommended for annual vaccination in the U.S. are a) groups that are at increased risk for influenza-related complications: persons aged 65 years or older, residents of nursing homes and other chronic-care facilities that house persons of any age who have chronic medical conditions; adults and children who have chronic disorders of the pulmonary or cardiovascular systems, including asthma; adults and children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications); children and teenagers (aged 6

Box 1: Recommended Case Definition for Influenza

Clinical case definition
A person with sudden onset of fever of >38°C and cough or sore throat in the absence of other diagnoses.

Laboratory criteria for diagnosis*
Virus isolation: Swab or aspirate from the suspected individual, **or** Direct detection of influenza viral antigen
Serology: Four-fold rise in antibody titre between early and late serum.

Case classification
Suspected: A case that meets the clinical case definition.

Confirmed: A case that meets the clinical case definition and is laboratory confirmed (used mainly in epidemiological investigation rather than surveillance).

**Rapid commercial diagnostic tests are available and are useful for outbreak investigations, but their sensitivity and specificity need to be better studied.*

months to 18 years) who are receiving long-term aspirin therapy and therefore might be at risk for developing Reye syndrome after influenza; and women who will be in the second or third trimester of pregnancy during the influenza season; b) the group aged 50-64 years because this group has an elevated prevalence of certain chronic medical conditions; and c) persons who live with or care for persons at high risk (e.g., health-care workers and household members who have frequent contact with persons at high risk and can transmit influenza infections to these persons at high risk). Vaccination of these high-risk groups has shown to be among the most cost-effective interventions in public health.

The ACIP recommendations described above have been the basis for influenza vaccination recommendations in most countries where this vaccine is provided. Depending on their epidemiologic characteristics, some countries may consider the vaccination of other high risk groups, including indigenous communities living in isolation. However, financial or logistic limitations can constrain some countries to limit the recommendations to the groups at highest risk or to those high-risk groups easier to identify.

Work absenteeism due to influenza could be a problem among otherwise healthy adults. Although this and other low-risk groups can also benefit from vaccination, C. Bridges and others, in a two years cost analysis of influenza vaccination in a work setting found that, from a public health perspective, there were no savings when giving the flu shot to healthy adults.

Flu vaccine

A person's immunity to the surface antigens reduces the likelihood of infection and severity of disease if infection occurs. Antibody against one influenza virus type or subtype confers limited or no protection against another influenza virus type or subtype. Furthermore, antibody to one antigenic variant of influenza virus might not protect against a new antigenic variant of the same type or subtype. Antigenic drift is the reason for the incorporation of one or more new strains in each year's influenza vaccine. It is also the basis for the recommendation of yearly influenza vaccination.

Because manufacturers need at least 6 months to prepare a new vaccine, the World Health Organization (WHO) meets every year (usually in March) to recommend the influenza strains to be included in the vaccine for the Northern Hemisphere's winter (usually December to March). Until 1998, the vaccine recommended for the Northern Hemisphere was used for the Southern Hemisphere winter half a year later. Studies by Regnery, Savy et al. have shown that, for eight out of ten winters analyzed, the vaccine recommended for the Northern Hemisphere did not match the strains that circulated during the following Southern Hemisphere winter. For this reason, since 1998, WHO holds a second yearly meeting (usually in September), to recommend influenza vaccine strains for the Southern Hemisphere. Because of the often-unusual patterns of virus circulation in these areas, deciding the best time for vaccination in tropical and subtropical areas is more challenging and needs to be studied on a case-by-case basis.

The Northern Hemisphere 2001-2002 trivalent vaccine virus strains recommended are A/Moscow/10/99 (H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Sichuan/379/99-like strains. Although the recommended optimal time period for vaccinating individuals is usually October-November in the Northern Hemisphere, due to delays in the manufacturing and distribution of the vaccine, the ACIP made the following recommendations regarding flu vaccination strategies for the upcoming flu season in the U.S.: For providers: 1) target vaccine available in September and October to those at high risk and health-care workers; and 2) continue vaccination through December and as long as vaccine is available. For the public: 1) if at high risk, seek vaccine in September or October, or as soon as it is available and throughout the season; and 2) if not at high risk, seek vaccine in November or later. The vaccine components recommended for the 2002 Southern Hemisphere's season are, in this opportunity, the same as those recommended for the 2001-2002 Northern Hemisphere season.

Antiviral agents

The use of influenza-specific antiviral drugs for chemoprophylaxis or treatment of influenza is an important adjunct to vaccination. However, antiviral medications are not a substitute for vaccination. Four currently licensed influenza antiviral agents are available in the United States: amantadine, rimantadine, zanamivir, and oseltamivir. Amantadine and rimantadine are chemically-related antiviral drugs effective for treatment and prophylaxis of influenza A but not influenza B viruses. Rimantadine has the advantage of fewer side effects than amantadine. Both drugs are available as generics. Zanamivir and oseltamivir are recently approved neuraminidase inhibitors with activity against both influenza A and B viruses. Both zanamivir and oseltamivir were approved for the treatment of uncomplicated influenza infections. Zanamivir is approved for treatment for persons over 7 years of age, and oseltamivir is approved for treatment for persons more than one year old and for prophylaxis of persons over 13. To be effective for treatment, antiviral drugs have to be used within 48 hours of onset of the respiratory symptoms.

Future issues

Live intranasal vaccine

A nasal spray flu vaccine has been shown in clinical tests to prevent influenza in healthy children. It consists of live, attenuated viruses that may have the advantage over the inactivated vaccine of inducing a broad mucosal and systemic immune response, ease of administration, and the acceptability of an intranasal, painless route of administration compared with injectable vaccines.

Although the United States Food and Drug Administration (FDA) has yet to complete its analysis of the product's safety, live, cold-adapted influenza vaccines such as this one have been in use in the former Soviet Union since the 1960s. It could become available in the United States for the 2002-2003 winter. In a recent study of children aged 15-71 months, an intranasally administered trivalent live, cold-adapted influenza vaccine was 93% effective in preventing culture-positive influenza infections and reduced otitis media among vac-

cinated children by 30% compared with unvaccinated children. In a follow-up study during the 1997-1998 season, the trivalent live, cold-adapted influenza vaccine was 86% effective in preventing culture-positive influenza among children, despite a poor match between the vaccine's influenza A(H3N2) component and the predominant circulating influenza A(H3N2) virus. A study conducted among healthy adults during the same season found a 9%-24% reduction in febrile respiratory illnesses and 13%-28% reduction in lost work days.

Should young children be recommended for vaccination?

Studies indicate that rates of hospitalization are higher among young children than older children when influenza viruses are in circulation. However, the interpretation of these findings has been confounded by cocirculation of respiratory syncytial viruses, which are a cause of serious respiratory viral illness among children and which frequently circulate during the same time as influenza viruses. Recent studies by Izurieta et al and by Neuzel et al have attempted to separate the effects of respiratory syncytial viruses and influenza viruses on rates of hospitalization among children under 5 who do not have high-risk conditions. Both studies indicate that otherwise healthy children under 2 years of age are at increased risk for influenza-related hospitalization compared with older healthy children. Because very young healthy children are at increased risk for influenza-related hospitalization, the ACIP is studying the benefits, risks, economic consequences and logistical issues associated with routine immunization of this age group in the U.S.

Source: Prepared by Dr. Hector Izurieta from PAHO's Division of Vaccines and Inmunization (HVP).

Diphtheria Outbreak in Cali, Colombia, August-October 2000

Background

The incidence of diphtheria has declined in recent years in countries such as Cuba, Canada, or the United States that have a functional vaccination program where effective coverage with diphtheria toxoid and Diphtheria-Tetanus-Pertussis (DTP) vaccines have been achieved, especially in the infant population. In addition to the reduction in incidence, a change in the epidemiological profile of the disease was also registered. Indeed, its marked predilection for infants and young children has shifted in the last decade, to involve more young and older adults. On another hand, although mortality has increased during pandemics, the relation of this phenomenon to the causes of the pandemics is not known. Hypothesis on these changes include possible transformations in the microorganism or in the host population that diminish the protective antibodies as age increases.

Santiago de Cali, the capital of the "Valle del Cauca" province, is located at 995 meters above sea level. The average temperature is 25 degrees Celsius. It is the city that attracts the most people in Southwestern Colombia. It has a population of two million people distributed in 20 urban and 3 rural districts ("comunas" or communes), with marked differences in their socioeconomic levels and living conditions.

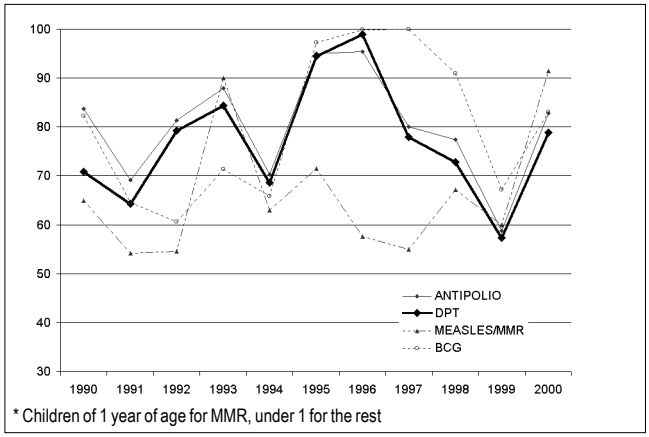
For health services delivery, Cali relies on a public network of institutions that are part of the local health systems (Silos), of which 6 are urban and one rural, and on "Empresas Promotoras de Salud", or health promoting companies, with their own network of services[a].

The Municipal Public Health Service is the regulatory entity for surveillance and control in the city. It follows the guidelines and policies laid out by PAHO/WHO and the Ministry of Health with regard to the activities of the Expanded Program on Immunization and Surveillance of vaccine-preventable diseases that are object of eradication, elimination and control. There exists a network of Reporting Units formed by all institutional health service providers.

The last diphtheria case recorded in Cali itself was in 1988. However, an outbreak occurred at the level of the province, in the municipality of Buenaventura, in 1992. On that occasion, a total of 88 people with symptoms compatible with diphtheria were examined. The ages ranged between 1 and 47 years. Laboratory tests were conducted in only 51 of these patients. The bacteriological results were as follows: virulent *Corynebacterium diphtheriae* was identified in 28 (54.9%) of the patients, and non-virulent *C. diphtheriae* was identified in 4 (7.8%) of them. Of the total of cases, 4 were fatal.

Figure 1 shows the coverage of a selection of vaccines in children under 1 year in Cali between 1990 and 2000. It can be observed that an increase in the coverage had been achieved between 1990 and 1996, but starting in 1997, the coverage began to decline until 1999, when they reached around 60% in all the biologicals shown here. The reasons for this decline cannot be determined with certainty without a more in-depth study of the factors that had an influence on the vaccination coverage. However, a possible factor in this

Figure 1: Vaccination Coverage for a Selection of Vaccines*, Cali 1990-2000



* Children of 1 year of age for MMR, under 1 for the rest

[a] The "Empresas Promotoras de Salud" are denominations created by law in the new Colombian Social Security System. They are companies that manage the ressources of their affiliates and beneficiaries.

decline may have been the change in the health services delivery in general - and of immunization in particular - introduced after the application of a law called "Ley 100" in Colombia. The purpose of this law, which was enacted in 1993, is to transform the old National Health System into a mixed general social security system with two contribution regimens (contributory and subsidized). Before 1997, when the new National Health System was consolidated, the public network was responsible for children immunization, which guaranteed an effective coverage with massive strategies, channeling and extramural activities. Starting in 1997, other actors of the social security system, among them nonprofit or for-profit private or semipublic companies, entered the network of service providers. Regardless of whether or not the vaccination services were appropriate in the years preceding the law, it is certain that the resulting change in services - shown by the vaccination coverage - does not meet the vaccination needs. This can explain in part the observed decline in coverage.

On the other hand, the economic crisis that affected the national and local health sector worsened in recent years and affected the Expanded Program on Immunization. This impact is reflected in the lack of supplies, and also resulted in the decline of vaccination coverage at the end of the 1990s.

Materials and results of the investigation

In 2000, an outbreak of diphtheria occurred in Cali between epidemiological weeks 30 and 42, with 8 confirmed cases. The first reported case was a 3 year-old girl. It was the only fatal case. A bacteriological study of a total of 458 suspected cases was carried out. Operational definitions used during the outbreak investigation can be found in Box 1. These cultures were completed for symptomatic persons who consulted health services spontaneously and to direct and indirect contacts of suspected cases. In 1.8% (8) of these samples, *C. diphteriae* was isolated with positive toxigenicity test. In 32 cases (7%), non-toxigenic *C. pseudodiphtheriticum* was isolated. No bacteria of the *Corynebacterium sp.* was found in the remainder of the patients. All clinically-compatible cases were confirmed by laboratory with isolation of the bacteria. The population under 20 was the most affected by the outbreak (65%).

Of the 8 confirmed cases, 75% were younger than 10 years of age and 25% were 11 to 18 years old. In addition, 5 cases were found in men and 3 in women. In 2 cases (25%) non-virulent *C. diphtheriae* was found and as a result they were classified as healthy carriers.

The death of the 3 year-old occurred in a neighborhood of a district located in the eastern part of the city. A total of 26 related contacts were found, who shared the same overcrowded dwelling and lived in precarious hygienic conditions - factors that led to the outbreak.

In spite of the immediate interventions that were carried out as part of the field investigation, 4 more cases with epidemiological link to the fatal case (brothers) were presented in weeks 31 to 34. In week 41, 2 cases (2 brothers) were reported, without epidemiological link to the previous ones. Those were located in a commune of the northeast of the city. This implies that there were multiple sources of infection, indicating the possibility that additional cases were not detected. The last case of the outbreak appeared in week 42, in a 19 year-old adolescent residing in a commune of the southeastern area of the city. It did not have any epidemiological link with any of the previous cases (Figure 2).

The case-fatality rate of the outbreak was of 12.5% (1/8). The proportional distribution by age was as follows: 25% (2/8) in the 0-4 years group; 50% (4/8) in the 5-9 years group, 12.5% (1/8) in the 10-14 years group, and 12.5% (1/8) in the 15-19 age group (Table 1). The proportion of vaccinated among the cases was 12.5% (1/8), at the expense of a child vaccinated with three doses of DPT. Of the cases, 62% had incomplete series of vaccination and 75% (6/8) did not have access to social security.

The 8 cases belong to a socioeconomic stratum characterized by a high percentage of unmet basic needs, shown in overcrowded dwelling conditions, unhealthy conditions, inadequate excreta disposal and difficult access to drinking

Box 1: Operational Definitions Used during the Outbreak Investigation

Suspected Case: Patient of any age with upper respiratory tract disease (pharynx, larynx, tonsils, nose), characterized by throat pain, light fever, which may be accompanied by adhering membrane and/or difficulty to swallow or breathe.

Confirmed Case: Symptomatic or asymptomatic case that is confirmed by isolation of toxigenic *Corynebacterium diphteriae*, or any suspected case that has an epidemiological link with a laboratory-confirmed case.

Contact: Any person living with a confirmed case, or frequenting his/her household or having some link (occupational, academic, social etc.) with a confirmed case.

Figure 2: Diphtheria Cases By Epidemiological Week, Cali, August-October 2000

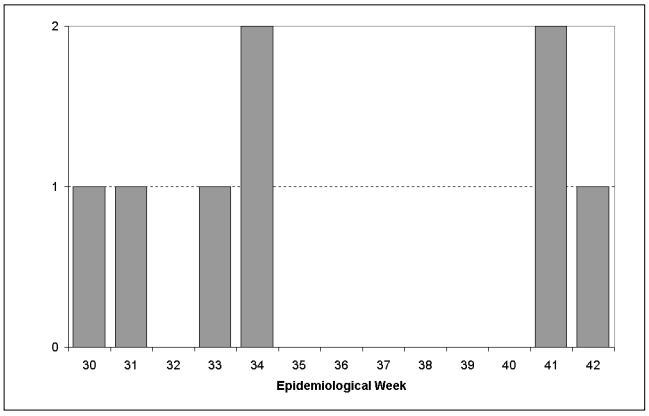


Table 1: Distribution of Diphtheria Cases by Age and Sex

Age	Sex M	Sex F	%	Rate x 100,000
0-4	0	2	25	14.8
5-9	3	1	50	31.2
10-14	1	0	12.5	31
15-19	1	0	12.5	31
Total	5	3	100	7.9

water and sewerage services. The clusters of cases were found in neighborhoods located in 3 urban communes of the city, all distant from one another.

Interventions

A plan with 7 strategic lines of action was designed: 1) Intensive vaccination activities in risk groups; 2) Monitoring and reporting of suspected cases; 3) Review and adaptation of the case management protocol; 4) Proper management of confirmed cases and contacts; 5) Timely laboratory diagnosis; 6) Mass communication campaign; 7) Interinstitutional and intersectoral coordination for case management and vaccination intensification.

At the beginning the outbreak, immediate hospitalization of all suspect cases that had had direct contact with the fatal case was put in place as a control measure, permitting effective control of the outbreak.

In the control plan, and in accordance with the patterns of the outbreak, it was determined that complete DPT vaccination series were to be carried out in all children under 5 showing incomplete vaccination and to the women of childbearing age from 10 to 49 years, target for the neonatal tetanus elimination plan. It was also decided to give priority to the vaccination with Td of schoolchildren (6 to 18 years), as this group was the most affected. A vaccination coverage of 80% was obtained in this group.

During the investigation, the design and implementation activities were carried out with participation of various institutions and sectors. Further, there was high community participation, and analysis was carried out on a constant basis, which allowed for periodic adjustments to the action plan. In spite of these positive elements, various difficulties arose, linked to the economic and political environments in the country. Firstly, adequate procurement of supplies (among them the diphtheric antitoxin) was complicated for various reasons, including importation processes. Further, a work-related crisis started in this period, due to lack of wage payments and processes of the administrative reform. This implied a decrease in human resources, especially on the operational side, as well as the creation of a situation of uncertainty and the appearance of a related lack of motivation. These circumstances had an impact on the completion of the control plan, which was continued into March 2001. At that time, it was evaluated and guidelines were produced for its continuity and the attainment of the proposed goals. Other difficulties included some delay in the accomplishment of the chronogram of the outbreak investigation activities and lack of clarity in the management of suspected cases with a *Corynebacterium* report.

Strict surveillance continued after the plan of operation concluded and no new case has been reported since October 2001, which suggests that the outbreak was successfully controlled.

Conclusions

Although one fourth of the cases occurred in people older than 10 years, the presence of cases in the group of 6-10 years suggests an accumulation of susceptible people that coincides with the low coverage found in recent years. A continued decline in the coverage could lead to the appearance of additional diphtheria outbreaks and to a change in the epidemiology of the disease, with a larger proportion of cases in unvaccinated children than in older adults. As a result, it is important to monitor and increase the vaccination coverage in the country.

The conditions of poor basic sanitation and overcrowding in which the persons affected by the outbreak lived led to the decision to hospitalize the symptomatic contacts. This was one of the most effective interventions in the control and management of the outbreak.

Source: Prepared by Ms. Nancy Landazabal García and Ms. María Mercedes Burgos Rodríguez from the Cali Health Secretary and Dr. Desirée Pastor from the PAHO/WHO Representation in Colombia.

Epidemiological Calendar

2002									
EW		S	M	T	W	Th	F	S	
1	Dec	30	31	1	2	3	4	5	Jan
2	Jan	6	7	8	9	10	11	12	Jan
3	Jan	13	14	15	16	17	18	19	Jan
4	Jan	20	21	22	23	24	25	26	Jan
5	Jan	27	28	29	30	31	1	2	Feb
6	Feb	3	4	5	6	7	8	9	Feb
7	Feb	10	11	12	13	14	15	16	Feb
8	Feb	17	18	19	20	21	22	23	Feb
9	Feb	24	25	26	27	28	1	2	Mar
10	Mar	3	4	5	6	7	8	9	Mar
11	Mar	10	11	12	13	14	15	16	Mar
12	Mar	17	18	19	20	21	22	23	Mar
13	Mar	24	25	26	27	28	29	30	Mar
14	Mar	31	1	2	3	4	5	6	Apr
15	Apr	7	8	9	10	11	12	13	Apr
16	Apr	14	15	16	17	18	19	20	Apr
17	Apr	21	22	23	24	25	26	27	Apr
18	Apr	28	29	30	1	2	3	4	May
19	May	5	6	7	8	9	10	11	May
20	May	12	13	14	15	16	17	18	May
21	May	19	20	21	22	23	24	25	May
22	May	26	27	28	29	30	31	1	Jun
23	Jun	2	3	4	5	6	7	8	Jun
24	Jun	9	10	11	12	13	14	15	Jun
25	Jun	16	17	18	19	20	21	22	Jun
26	Jun	23	24	25	26	27	28	29	Jun
27	Jun	30	1	2	3	4	5	6	Jul
28	Jul	7	8	9	10	11	12	13	Jul
29	Jul	14	15	16	17	18	19	20	Jul
30	Jul	21	22	23	24	25	26	27	Jul
31	Jul	28	29	30	31	1	2	3	Aug
32	Aug	4	5	6	7	8	9	10	Aug
33	Aug	11	12	13	14	15	16	17	Aug
34	Aug	18	19	20	21	22	23	24	Aug
35	Aug	25	26	27	28	29	30	31	Aug
36	Sep	1	2	3	4	5	6	7	Sep
37	Sep	8	9	10	11	12	13	14	Sep
38	Sep	15	16	17	18	19	20	21	Sep
39	Sep	22	23	24	25	26	27	28	Sep
40	Sep	29	30	1	2	3	4	5	Oct
41	Oct	6	7	8	9	10	11	12	Oct
42	Oct	13	14	15	16	17	18	19	Oct
43	Oct	20	21	22	23	24	25	26	Oct
44	Oct	27	28	29	30	31	1	2	Nov
45	Nov	3	4	5	6	7	8	9	Nov
46	Nov	10	11	12	13	14	15	16	Nov
47	Nov	17	18	19	20	21	22	23	Nov
48	Nov	24	25	26	27	28	29	30	Nov
49	Dec	1	2	3	4	5	6	7	Dec
50	Dec	8	9	10	11	12	13	14	Dec
51	Dec	15	16	17	18	19	20	21	Dec
52	Dec	22	23	24	25	26	27	28	Dec

As in previous years, we are including the Epidemiological Calendar for easy reference and use.

The Epidemiological Calendar includes the 365 days of the year, which are grouped in 52 weeks. Its use during surveillance activities is important because by standardizing the time variable, it provides a means to compare events that occur in a given year or during a specific period to others occurring at a later time or in other countries.

The 2002 epidemiological calendar begins on the 30th of December 2001. This is due to the fact that 1) the epidemiological weeks all start on Saturday, and 2) to determine the first epidemiological week of the year, we must choose the first Saturday in January that follows four or more days in January. Consequently, the first epidemiological week of 2002 starts on Sunday 30 December 2001 and ends on Saturday 5 January 2002.

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