Recent Advances in Diagnosis and Treatment of Venereal Diseases

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THE VENEREAL DISEASES, particularly syphilis and gonorrhea, and to a lesser degree the minor venereal diseases, chancroid, granuloma inguinale, and lymphogranuloma venereum, are still major public health problems. From 1957 through 1961 a marked increase occurred in reported cases of early infectious syphilis (primary and secondary) and gonorrhea. As shown in the table on page 612, the minor venereal diseases showed a decrease in reported cases from 1957 to 1960, but an increase in 1961 (*1*).

Perhaps if private physicians are alerted to the increasing incidence of early infectious syphilis, they will become more suspicious regarding the possibility of this infection in their patients.

The following review of the diagnosis and management of syphilis and gonorrhea, summarizing selections from recent literature, provides a ready reference.

SYPHILIS

The stages of syphilis and the objective findings of these stages are:

Primary. The patient has a genital or extragenital chancre (sometimes more than one), varying from pinpoint size to several centimeters in diameter and usually painless. Genital chancres often have a satellite inguinal bubo. All male patients should be examined for chancre of the anorectal area. Serum from the lesion is dark-field positive and serologic tests for syphilis may be either reactive or nonreactive. The patient has a history of exposure within the past 3 months. The primary stage lasts from a few weeks to about 3 months in the untreated patient.

Of particular interest to the urologist is the intra-urethral chancre, which may be overlooked in male patients. Dr. Elgin of Miami, Fla., reported that among 185 males treated for primary and secondary syphilis from 1957 to 1961, 14 had intra-urethral chancres (*2*).

Clinically, the intra-urethral lesions are painless, and they have a firm induration. Depending on the size and the amount of induration of the lesion, the appearance of the urethral meatus is altered; the orifice can be dry and gaping, patchy or inflamed, and edematous. The urethral lumen is usually narrowed and can partially alter the normal urinary stream. Usually, the patient has a urethral discharge which is serosanguineous, seromucoid, or thin, watery, and scant. The discharge, even when it is also associated with a gonorrhea infection, is usually not very profuse. The inguinal lymph nodes are enlarged and indurated, but not painful.

A diagnosis of intra-urethral chancre is often missed because the urethra is not palpated. Any male with a urethral discharge, or named as a sex contact of a person with early infectious syphilis, and who has no visible penile or rectal lesions, should be suspected of having a

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primary lesion of the balanic portion of the urethra. On palpation of the ventrodorsal portion of the glans penis, if an endo-urethral lesion is present, a very firm, painless induration extending 1 or more centimeters in depth within the meatal orifice can be felt. The induration is often missed when the glans is palpated laterally. Application of steady pressure while palpating the glans will cause an increase of serosanguineous discharge, which may be used for dark-field examination. Syphilis should also be suspected when indurated, nonpainful inguinal lymph nodes are felt on palpation. Satellite buboes seldom occur when the urethral discharge is due to gonococcus or to a nonspecific urethritis.

Secondary. Clinical evidence of this stage may include syphilitic alopecia areata of the scalp, annular or oval lesions on the face, forehead, chin, and neck; mucous patches in the mouth; and a nonpruritic generalized maculopapular rash which also appears on the palms of the hands and soles of the feet. Condylomata are present on the external genitalia and anal area. Serum from the lesions is dark-field positive and serologic tests for syphilis are reactive with a high titer. This stage lasts from 3 to 6 months in the untreated patient.

Early latent and late latent. These stages are asymptomatic. Early latent infection is of less than 2 years' duration, and late latent more than 2 years. Serologic tests for syphilis are reactive.

Late. This stage occurs from 5 to 20 years following the primary stage in an untreated patient. The systems affected are: cardiovascular, central nervous, bone, skin, or visceral. Serologic tests for syphilis are reactive.

Congenital. Early congenital syphilis is of less than 2 years' duration, and late congenital syphilis is of more than 2 years' duration. Serologic tests for syphilis are reactive.

Laboratory Tests

During the primary and secondary stages, *Treponema pallidum* in the serum from a lesion can be demonstrated by means of a dark-field microscope.

Other tests developed for the diagnosis of syphilis are briefly described below.

Serologic Tests for Syphilis (STS)

In response to invasion by the *Treponema pallidum*, reagin (an antibody complex) appears in the serum of the syphilitic person, usually 4 to 6 weeks after infection, or 1 to 3 weeks after the primary chancre appears. The presence of reagin in the patient's serum is measured by serologic tests for syphilis using nontreponemal antigens that are made from beef heart rather than from *T. pallidum.*

Reagin tests are of two types: (*a*) flocculation, of which the most commonly used are the VDRL, Mazzini, Kahn, and Kline; and (*b*) complement fixation, most often the Kolmer test. These nontreponemal tests are not absolutely specific or sensitive for syphilis. However, they are quite practical and highly indicative.

The sensitivity of a test refers to its ability to be reactive in the presence of syphilis, while specificity refers to its ability to be nonreactive in the absence of syphilis.

Laboratory reports based on sensitivity and specificity tests are qualitative and quantitative. The qualitative report merely indicates the presence or absence of reagin. The quantitative report is more useful in evaluation of treatment. If the titer is established before treatment, its

Total cases of venereal diseases reported in the United States, 1957–61

Year	Total syphilis	Primary and secondary syphilis	Gonorrhea	Chancroid	Granuloma inguinale	Lymphogranuloma venereum
1957	130, 552	6, 251	216, 476	1, 860	348	449
1958	116, 630	6, 661	220, 191	1, 574	332	436
1959	119, 981	8, 178	237, 318	1, 604	282	485
1960	120, 249	12, 471	246, 697	1, 555	273	800
1961	125, 262	18, 781	265, 665	1, 595	296	842

descent indicates response to treatment. If the patient was treated adequately before the chancre appeared or in the seronegative primary stage, the STS will remain nonreactive. If the patient was treated in the seropositive primary stage, the STS will become nonreactive in about 6 months. If treated in the secondary stage, the STS will become nonreactive in 12 to 18 months.

Special Nontreponemal Screening Tests

The four tests mentioned below are intended for screening only. If a test is reactive, a venous specimen should be drawn and processed for the standard serologic tests, such as the VDRL slide test.

Rapid plasma reagin test (RPR). This tests unheated plasma rather than serum, using a modified VDRL antigen which is made more sensitive by choline chloride. The blood is collected in anticoagulant tubes (with oxalate, sequestrene, or heparin), centrifuged, and tested immediately (*3*).

RPR card test. A recent modification of the RPR test, this tests a few drops of blood from the finger without the use of laboratory apparatus. A drop of blood is placed on a chemically treated card. The serum is collected and transferred to a second card. One drop of antigen is added. The results are read macroscopically. Reactive specimens show clumping of black specks, and nonreactive specimens show no clumping after 4 minutes. This kit is now commercially available (*4*).

Plasmacrit (PCT). This is an adaptation of the RPR test which performs a similar test on the plasma portion of a micro-hematocrit determination. After the cell volume is read, the capillary tube is nicked and divided. The plasma is drawn into a smallpox-vaccine rubber bulb and tested on a slide with RPR antigen (*5*).

Unheated serum reagin test (USR). Another modification of the RPR test, this test substitutes unheated serum for plasma. (*6*).

Treponemal Antigen Tests

Antigens used in nontreponemal tests are not entirely specific for syphilis. However, antigens prepared from treponemes produce a specific test. Syphilitic antibodies appear in the blood much later than reagin does. Since treponemal tests are reactive later in early syphilis, it is possible to have a nonreactive result in some cases of early syphilis.

Tests using *T. pallidum* (Nichol's strain) or extracts from this treponeme are listed below (*7*).

Whole Body Antigen

Viable organisms:
- *Treponema pallidum* immobilization (TPI)
- *Treponema pallidum* methylene blue (TPMB)

Usually nonviable organisms:
- *Treponema pallidum* agglutination (TPA)
- *Treponema pallidum* immune adherence (TPIA)
- Whole body *Treponema pallidum* complement fixation (WTPCF)
- Fluorescent treponemal antibody (FTA)

Fraction of Organisms as Antigens
- *Treponema pallidum* complement fixation (TPCF)
- Treponemal Wassermann reactive (TWR)
- *Treponema pallidum* cryolysis protein (TPCP)

The TPI test uses as the antigen *T. pallidum* obtained from rabbits with syphilitic orchitis. The treponemes are kept alive for a few hours in a special medium. When syphilitic serum and complement are added and incubated, the treponemes are immobilized. The TPI test is helpful in ruling out biologic false-positive results, but it is expensive to perform. The TPCF test is less expensive and can be done in any laboratory equipped to perform a complement fixation test.

The FTA test uses *T. pallidum* and fluorescein-tagged antibodies. In evaluation studies this test has proved more sensitive than, and as specific as, the TPI test. These two tests react to similar or to the same antibodies.

Reiter protein complement fixation (RPCF). This test uses an antigen prepared from a nonpathogenic treponeme (Reiter). It is also known as the Kolmer test with Reiter protein antigen (KRP) because the one-fifth Kolmer complement fixation procedure is used with the Reiter protein fraction. Treponemal antigen tests which use extracts from the Reiter treponeme are easy to perform and they are relatively inexpensive.

Treatment

Penicillin is the best known drug for the treatment of syphilis. A penicillin blood level, ranging between 0.03 and 0.2 unit per milliliter,

maintained over a period of 10 days is adequate treatment for any stage of syphilis. Adequate treatment can be effected by a number of schedules using penicillin preparations, as shown below (*7*).

Abortive, Primary, Secondary, Early Latent, and Late Latent Syphilis

Benzathine penicillin G (Bicillin): A long-acting repository penicillin which maintains blood levels from 4 to 6 weeks. The total dose is 2,400,000 units with 1,200,000 units injected in each buttock in one visit.

Procaine penicillin G with 2 percent aluminum monostearate (PAM): Maintains blood levels from 3 to 4 days. A total of 4,800,000 units; 2,400,000 units at first visit, and 1,200,000 units at each of two subsequent visits 3 days apart.

Aqueous procaine penicillin G: Used when daily injections are indicated or desired. A total of 4,800,000 units; 600,000 units daily for 8 days.

Alternate antibiotics: For patients who are sensitive or allergic to penicillin, terramycin or erythromycin are the best alternates. Terramycin is given daily in 1- to 2-gram doses for a total dosage of 30 to 40 grams. Erythromycin is given daily in 1- to 2-gram doses for a total dosage of 20 to 30 grams.

Late Syphilis

Benzathine penicillin G (Bicillin): A total of 6 to 9 million units; 3 million units at weekly intervals.

Procaine penicillin in 2 percent aluminum monosterate (PAM): A total of 6 to 9 million units; 1.2 million units at 3-day intervals.

Aqueous procaine penicillin G: A total of 6 to 9 million units; 600,000 daily.

Early Congenital Syphilis

Benzathine penicillin G (Bicillin): 50,000 units per kg. of body weight in a single injection.

Late Congenital Syphilis

The same schedules are recommended as those for early infectious syphilis.

GONORRHEA

The male patient with a urethral discharge and with a diagnosis confirmed by smear and culture may not always respond to treatment with dosages of penicillin ranging from 300,000 units to 900,000 units of PAM. When this condition occurs, the physician is faced with a diagnostic problem as the cause may be due to one of the following:

Reinfection. The patient may have become re-infected by exposure during the incubation period following his first dosage of antibiotic, especially when the exposure has been to a known case.

Inadequate dosage. Dosages of less than 600,000 units of penicillin are inadequate and in some instances 900,000 units may be inadequate.

Outdated penicillin. This has a markedly reduced potency, and its effect on the patient is the same as that of an inadequate dosage.

Penicillin-resistant gonorrhea. Resistance of the gonococcus to penicillin can be determined by penicillin sensitivity tests on specimens from the patient.

Penicillinase. The patient should be carefully examined for staphylococcal infection, which may have escaped detection. Staphylococci will neutralize somewhat the effects of penicillin.

Mimeae. Patients with confirmed gonorrhea who have a persistent discharge after penicillin therapy are often accused of reinfection or of having penicillin-resistant strains of gonococci. It is possible that many of these patients harbor a bacteria known as the tribe of Mimeae, which imitates the gonococcus of Neisser and which is resistant to penicillin. It is extremely difficult to distinguish the Mimeae from the gonococci, and differentiation requires elaborate culture techniques.

The tribe Mimeae is composed of a group of organisms characterized bacteriologically by (*a*) gram negativeness with some tendency to retain the violet stain; (*b*) pleomorphism with the diplococcoid forms predominating on solid media; (*c*) a modified type of bipolar staining; (*d*) encapsulation; and (*e*) a characteristic colonial appearance in certain media.

The tribe comprises three genera which are differentiated primarily by their reactions to fermentation. The genus *Mima*, with a single species *M. polymorphia*, has oxidase-positive and oxidase-negative varieties which do not produce acid from any of the usual carbohydrates tested. The genus *Herellea*, with a single species, *H. vaginicola*, produces acid with no gas from certain carbohydrates; and the genus *Colloides*, with a single species *C. anoxydana*, produces both acid and gas from certain carbohydrates.

Treatment for infection with Mimeae con-

sists of 1 gram daily of either terramycin or erythromycin for a total dosage of 3 to 5 grams.

Laboratory Tests

All persons infected with, suspected of having, or exposed to gonorrhea should receive a routine serologic test for syphilis.

Conventional Culture

Conventional culture procedures for identification of *Neisseria gonorrhoeae* in females, although superior to other current methods, are slow, cumbersome, and costly to perform. Consequently, these procedures have been abandoned in many laboratories.

Reports from large venereal disease clinics indicate that standard culture methods, performed under most favorable circumstances, were able to detect gonococcus in only 16 to 47 percent of female contacts of males with gonorrhea.

Fluorescent Antibody (FA) Tests

The fluorescent antibody technique for detection of the gonococcus has been described by Dr. W. E. Deacon of the Venereal Disease Research Laboratory, Public Health Service (*8*). The preparation and use of fluorescein-labeled antiserums for the detection of the gonococcus in males was reported in the same year. The FA technique can be applied to the detection of most bacterial strains and some viruses.

In a study by the Fulton County Health Department, Atlanta, Ga., of female contacts of infected males, the direct and the delayed methods of the FA technique were used, as described below (*9*).

Direct method. Specimens were obtained from the urethral, vaginal, and cervical sites, using sterile, cotton-tipped applicator sticks. Duplicate slides were prepared for smears from each site. Smears were fixed and stained with fluorescein-labeled antiserum for 1 hour at 37° C. Leitz and Reichert ultraviolet light microscope assemblies were used for determining fluorescents. A desirable contrast between background and specific *N. gonorrhoeae* fluorescents was obtained by the proper selection of filters. A blue background was used to define the gonococcus in an intracellular position.

Delayed method. Slants were prepared from Difco GC medium base plus hemoglobin and supplement B. This medium was placed in 15- by 125-mm. tubes. Specimens were collected by means of sterile cotton-tipped applicator sticks, as described for the direct FA procedure. Slants were inoculated immediately after specimen collection by rotating and rubbing the swab over the surface of the medium. The stick was then broken so that the cotton swab remained in the tube, supported by the butt. After inoculation, slants were immediately placed in a candle jar and held at room temperature until subsequent inoculations were performed from another patient, at which time the jar was again opened.

After completion of specimen collections (4–6 hours) candle jars were incubated for 16–20 hours at 35° C. Slant growth was mixed by the original swab left in the tube. This swab was also used to prepare heavy smears which were allowed to air-dry. All delayed FA smears were fixed for 10 minutes in 3 percent formalin in phosphate buffered saline pH 7.2. This was followed by a distilled water rinse. Slides were finally blotted and allowed to air-dry. Subsequent staining with fluorescent antibody and microscope observation were the same as for the direct FA.

Both the direct and delayed FA methods have an advantage over the conventional culture method. The direct FA method can be done in 1 hour, whereas the conventional methods, including sugar fermentation, frequently require 10 or more days to complete. The delayed FA method gives a greater yield of positive results in less time than the conventional culture method. The delayed technique is superior to that of the direct method.

Treatment of Males

Uncomplicated gonorrhea. Benzathene penicillin G (Bicillin) or procaine penicillin G in 2 percent aluminum monostearate (PAM), 900,000 units in one injection.

With complications (conjunctivitis, prostatitis, arthritis). Aqueous penicillin G, 1,200,000 units at 2-hour intervals until symptoms

have subsided, plus 1,200,000 units Bicillin in one injection.

Retreatment. If discharge in uncomplicated gonorrhea persists for 3 or more days after initial treatment and smear or culture is still positive, retreatment with 1,200,000 units Bicillin plus 900,000 units PAM in one injection is recommended.

Treatment of Females

All female sex contacts of males with gonorrhea should be given prophylactic penicillin therapy even when gonococci are not demonstrated in urethral, cervical, or vaginal smears.

Females with confirmed gonorrhea or those named as contacts should receive 1,200,000 units Bicillin plus 900,000 units PAM in one injection.

Alternate Treatment

For all patients who are allergic or sensitive to penicillin, selection of one of the following schedules is recommended: (*a*) oxytetracycline (terramycin), 0.5 gram orally every 4 hours for a total of 2 grams; (*b*) streptomycin or dihydro-streptomycin, 1 gram in ½ cc. of sterile distilled water or saline in one intramuscular injection; or (*c*) chloramphenicol, 0.5 gram orally every 4 hours for a total of 2 grams.

Penicillin Sensitivity

Patients who are allergic to penicillin can be detected by a history of penicillin sensitivity or by skin testing with penicillin G. Conjunctival, scratch, and intradermal tests have been widely advocated.

The usual skin-testing techniques require special preparations of various dilutions of penicillin. Although these tests are significant only when positive, a negative test is no guarantee against a subsequent reaction.

A newer skin-testing technique, using penicilloyl-polylysine, was performed by Dr. Jack Shapiro of the St. Louis (Mo.) Health Department on 3,687 patients in the venereal disease clinic (*10*). A correlation of the results with the patients' histories revealed that 117 patients with a previous history of penicillin sensitivity and 165 patients with no history of penicillin sensitivity had positive skin tests. These patients were given one of the broad-spectrum antibiotics rather than penicillin. Twenty patients with a previous history of penicillin sensitivity and 3,385 patients with no history of penicillin sensitivity had negative skin tests. They were given penicillin, and no reactions occurred among them.

The results of the study indicate that use of penicilloyl-polylysine as a skin-testing preparation to determine hypersensitivity of patients to penicillin seems to be fairly accurate and without apparent danger to the patient.

Discussion

Physicians should report all patients with confirmed venereal disease to their local health departments. This information provides the health officer with an index to the incidence and prevalence of disease in the community. Also, in order to break the chain of infection, these patients should be interviewed for sex contacts. If the private physician is unable to take time to get the names, addresses, and other pertinent information concerning contacts, the health department will provide this service for him. All interviews are confidential and the informant's name is never revealed to the contact. The physician's permission is required before a health department representative can interview a patient.

Complete cooperation of all medical facilities is required to eradicate venereal disease. This can be accomplished by good diagnosis, adequate treatment, prompt reporting of cases to the health department, and interviewing of all infected persons.

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Education Notes

Home Teachers for the Adult Blind. A 16-month graduate course leading to a master's degree for home teachers of the adult blind will open in September 1963 at Western Michigan University, Kalamazoo. The project, supported by a Federal grant from the Vocational Rehabilitation Administration, follows a nationwide study of home teaching of the adult blind.

Candidates who wish to be considered should apply to Prof. Donald Blasch, Director, Program for Training Home Teachers for the Blind, Western Michigan University, Kalamazoo, Mich.

Houseparent Training. Traineeships for houseparents are offered in a 12-month full-time course in specialized child care services at the Devereux Schools, a private residential treatment center in suburban Philadelphia. The program emphasizes work with mentally retarded and emotionally disturbed children and maladjusted adolescents.

Applicants should have at least a high school education and like children. Those with experience in working with children will be given preference. Applicants with more education and experience will have opportunities for advanced training.

Trainees will receive tuition, books and supplies, room and board, and tax-exempt stipends of $100 to $150 per month. Further information and application blanks are available from Dr. Henry Platt, Director of Training, Devereux Foundation Institute for Research and Training, Devon, Pa.

Care of Premature Infants. In the fall of 1963, the institutes for physicians and nurses in the care of premature infants at the New York Hospital-Cornell Medical Center, under the sponsorship of the New York State Department of Health and the U.S. Children's Bureau, will begin their 15th year of operation. The institutes are designed to meet the needs of physicians and nurses in charge of hospital premature nurseries and special premature centers and of medical and nursing directors and consultants in State and local premature programs.

Attendance at each institute is limited to six physician-nurse teams. The program for physicians lasts 2 weeks; the one for nurses, 4 weeks. Participants pay no tuition fee, and stipends are provided to help cover expenses during attendance.

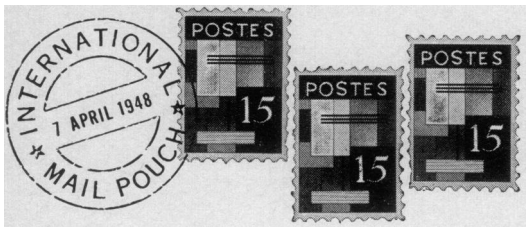
Institutes for the 1963–64 year are scheduled to start on September 16, November 11, January 6, March 16, and May 11. Early application is essential since plans are contingent on the number of applications received.

Additional information may be obtained by writing Box 143, Institute in the Care of Premature Infants, New York Hospital, 525 East 68th Street, New York 21, N.Y.

Occupational Diseases From Animals. On January 7–9, 1964, the School of Public Health of the University of Michigan in Ann Arbor will sponsor an institute at the university on occupational diseases acquired from animals. Institute participants will consider the etiology and epidemiology of the viral, rickettsial, bacterial, protozoal, and helminthic diseases presenting occupational hazards in the United States.

On January 10, 1964, a 1-day meeting at the university, sponsored by the Institute of Laboratory Animal Resources of the National Academy of Sciences-National Research Council, will consider in greater depth animal diseases constituting a hazard to laboratory workers, with emphasis on specific dangers and control techniques.

Additional information may be obtained from Dr. Harold J. Magnuson, Professor of Industrial Health, Room W5634, University Hospital, Ann Arbor, Mich.



Mass Drug Treatment Against Malaria

Mass antimalarial drug treatments will begin among selected groups of persons in Costa Rica and Guatemala this year in accordance with an agreement signed by the governments of the two countries and the Pan American Sanitary Bureau, Regional Office of WHO.

The drugs will be administered to groups in Puntarenas Province, Costa Rica, and in Escuintla and Jutiapa Departments in Guatemala, where transmission of malaria persists despite regular spraying against the vectors of the disease. The two governments will be responsible for the daily administration of the projects, and the Bureau, which has budgeted $246,932 for them in 1963, will provide technical assistance.

Nutrition Gains in Japan

Since 1950, the nutritional status of the Japanese people has shown a gradual improvement, particularly in the average daily intake of protein, fat, and carbohydrate, according to a report by Minoru Muramatsu, Department of Public Health Demography, published in the December 1961 issue of the *Bulletin of the Institute of Public Health*, Tokyo.

The most striking changes were in the increased consumption of certain types of foods. From 1949 to 1959, consumption of milk and milk products soared 700 percent; eggs, 520 percent; meat, 340 percent; fat and oil, 320 percent; and fruits, 300 percent.

National nutrition surveys conducted by the Japanese Government also showed that although the average daily calory intake rose only slightly, from 2,097 in 1949 to 2,118 in 1958, consumption of animal protein increased from 14 to 24 grams in the same period and now comprises more than 30 percent of the total protein intake of the population.

Because of serious food shortages from 1940 to 1946, the average heights and weights for various age groups recorded in 1947 were low compared with 1937–38, but by 1952 they had reached prewar levels except in the age group 12–15 years. From 1952 to 1960, the average height of boys of 14 years increased 4.1 centimeters, their weight by 2.86 kilograms. Girls of the same age showed increases of 1.7 centimeters in height and 2.93 kilograms in weight for the 1952–60 period.

Muramatsu attributed the improved diet and a growth of interest in nutrition partly to changing population trends. The present stage is characterized by low fertility and low mortality, with a growth rate of less than 1 percent per year. During the 1947–60 period, the rate of natural increase dropped from 19.7 per 1,000 population to 9.6, the birth rate from 34.3 per 1,000 to 17.2, and the death rate from 14.6 per 1,000 to 7.6.

Bolivia's Antismallpox Campaign

A 3-year nationwide campaign to vaccinate 3 million Bolivians, 86 percent of the population, against smallpox will begin this year as the result of an agreement signed by the Pan American Sanitary Bureau and the government.

The Bureau, Regional Office for the World Health Organization, has allocated $60,000 for technical assistance, vehicles, and equipment and for fellowships to train Bolivian public health workers in eradication techniques in schools abroad. Bolivia will spend $78,000 in local currency in addition to the salaries of 53 of its permanent public health workers assigned to the campaign. Additional health workers will help when needed in the principal cities. Bolivia's National Institute of Hygiene will manufacture the dried vaccine to be used in the campaign.

In 1958 almost 80 percent of the population of Bolivia was vaccinated, and the number of cases of smallpox reported dropped from a yearly average of 604 between 1946 and 1957 to 7 in 1959, 1 in 1960, and zero in 1961. However, about 700,000 persons living in almost inaccessible areas were not vaccinated and, despite a population increase of 140,000 since 1958, only 64,000 additional vaccinations have been performed.

In the entire hemisphere, the number of cases of smallpox increased in 1962, with 2,928 reported from seven countries, compared with 1,939 from five countries in 1961. The 1962 total comprised 2 cases, Argentina; 2,672, Brazil; 1, Canada; 30, Colombia; 202, Ecuador; 10, Uruguay; and 11, Venezuela.