Epidemic of Variola Minor in a Suburb of São Paulo

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VARIOLA is endemic in the city of São Paulo, Brazil, and it occurs, usually on the outskirts of the city, in epidemics of limited spread in the neighborhood where this infection is introduced. This paper describes one of these small epidemics and the virus and antibody study of cases and contacts. Clinical findings, including distribution among clinical types and age and immunity-status groups, have been reported (*1*). The epidemic of 54 cases can be classified clinically as one of variola minor (alastrim).

The Epidemic

In June 1956, the daily newspapers reported nine cases of variola in the district school of Vila Guarani, a semi-isolated workers' residential district of São Paulo city. The allegation that the outbreak was limited to the school population was challenging since pupils did not reside in the school, attending it for only 3 hours a day. A casefinding survey disclosed that besides the nine cases reported to health authorities by the school teachers, other cases had occurred among the district's population and, particularly, in the households of the school children. Most of the unreported cases had been missed because of the mildness of the disease; also because of lack of knowledge and poverty, the families did not request medical attention.

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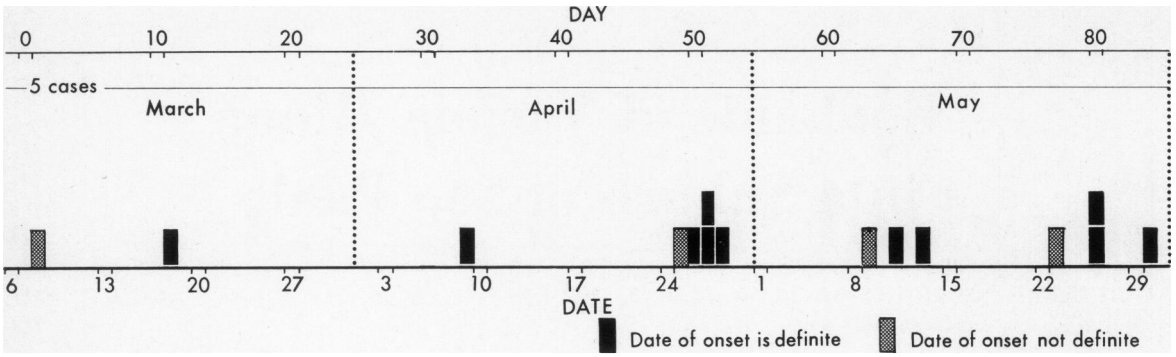
The epidemic had its onset during the second half of March 1956. Two travelers from northern Brazil arrived at Vila Guarani with clinical manifestations of variola. These two persons stayed for 9 days at the home of relatives, and then, when their cutaneous lesions had not yet reached the crust stage, they traveled to a locality in São Paulo State. From the home where these two had stayed, the infection spread first to a neighboring household and from there was introduced in the school where it spread among school children and in other households. During a casefinding survey, which started in early June and ended in the middle of September, dates of illness onset and of rash onset were established in most cases, and the probable source of contagion was investigated through inquiring about personal associations of persons known to have had variola recently. It was possible to trace practically the whole chain of contagion from onset of the epidemic in March 1956 to its end 5 months later.

The chart shows the chronologic distribution of cases which evidences a tendency to grouping of cases at regular intervals. The two introducers of variola to the district are included in the chart, which also shows the spread of infection to the city of Rio de Janeiro, some 400 kilometers distant from São Paulo city. On June 16, a household contact left for Rio de Janeiro in an attempt to escape from variola which was occurring in her Vila Guarani home. On June 19 in Rio de Janeiro, she showed the onset of variola which apparently provoked six cases in the household she joined.

Although some cases occurred during April and May among the children attending the school, it was not until early June that the

Onset of illness in 54 cases of variola minor



visiting nurse and some teachers noticed the disease and reported it to the São Paulo City Health Department. The department decided on mass vaccination which was compulsory for school children, while only a part of the district population submitted to vaccination. On June 30, the school was closed for the regular July vacation, during which the epidemic sharply declined. No home with cases was quarantined or subjected to current or terminal disinfection.

Twelve of the 54 patients with illness recorded were admitted to the distant Emilio Ribas Isolation Hospital. The cases of these 12 comprised almost all those reported to the health department, and the patients were isolated when the exanthem had appeared. Transmission to contacts may have already occurred. The remaining persons with illness were not isolated nor were any of the household contacts of patients. Many persons while in the exanthem stage walked freely in the district streets or attended the district school. Yet the epidemic did not spread much, as was evidenced by the findings of the exhaustive casefinding survey.

Identification of the Epidemic

Identification of the infection responsible for the epidemic was established, beyond any reasonable doubt, through the following evidence.

1. Characteristic of variola were the individual morphology of skin lesions; the body distribution of pocks, especially their presence on palms and soles; the constant occurrence of a prodromic period; the constant symptomatology and duration of the prodromic period even in benign cases; and the clinical course.

2. Only variola virus was isolated and identified in skin lesion specimens, and all the identifications were positive.

3. The antibody response of patients and contacts of patients indicated a recent infection with variola or vaccinia virus, and in all instances, the previous experience with these viruses had occurred too long ago to justify the present positive complement fixation found in serums.

4. Many patients were unvaccinated while most of the remainder had been vaccinated successfully a long time before.

5. No evidence of illness was observed among several household contacts who had variola in the past, not even among those who had not been vaccinated.

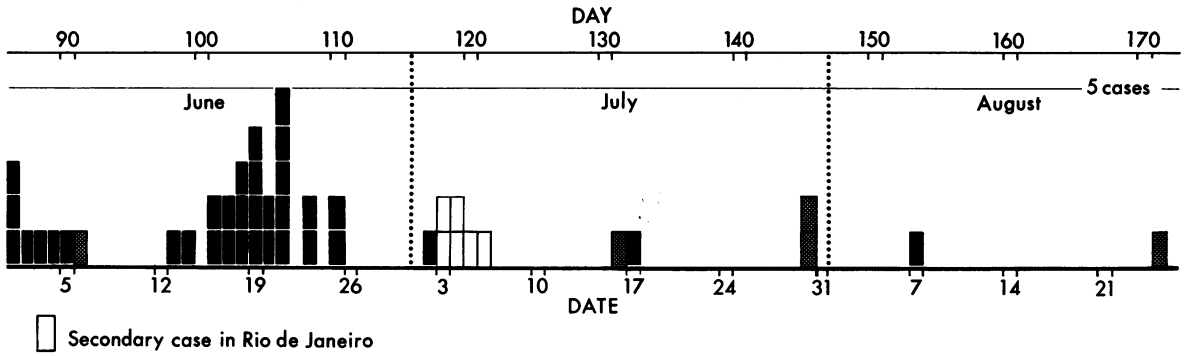
6. The majority of patients had chickenpox previously.

7. No typical case of chickenpox or any other exanthematous disease was observed during the epidemic period among the population at risk, nor was an epidemic of these or other diseases recognized in the district during this interval.

Virus and Antibody Study

Fluid content or crusts from several pocks were pooled in a tube containing 0.5 ml. of sterile broth; 15 of these pools were obtained from 7 persons. Saliva specimens were collected from seven persons as well as from five asymptomatic household contacts. Saliva was placed directly in an empty sterile tube. Specimens for virus isolation or serums separated from blood were kept at −25° C. until assay. Penicillin and streptomycin were added to saliva and skin lesion material before inocula-

in São Paulo and Rio de Janeiro, Brazil, 1956



tion onto the chick embryo chorioallantois. Identification was made by the morphology of membranal plaques (*2*), including histological examination and inoculation of isolates onto the rabbit skin (*3*) and cornea (*4*).

In the district school, collection of blood samples was limited to 18 children unsuccessfully vaccinated during the school outbreak because of the impossibility, due to a known group reaction (*5*), of differentiating between the response to vaccinia and variola viruses in children successfully vaccinated. In the households, a blood sample was collected from each of 10 patients and 19 of their contacts who had not recently been vaccinated. Because of limitations in the facilities available, only one blood sample was collected from each donor. The complement fixation and hemagglutination inhibition tests for antibodies against variola virus followed procedures (*6, 7*) based on standard techniques such as those of Kolmer and Boerner and Salk, respectively. Antigens were prepared according to McCarthy and Downie (*5*) using the Instituto Butantan's strain of vaccinia virus.

Virus in Pathological Material

Variola virus was isolated and identified in all 15 specimens of skin lesions. The isolated strains did not provoke chorioallantoic plaques whose morphology varied according to the severity of symptomatology in the patient from whom they were isolated. It should be stated, however, that this point was not subjected to purposeful analysis, the specimens having been discarded since they were obtained only to support clinical and epidemiologic diagnoses during the epidemic. Thus, the previous observation is the result of routine isolation work. The same morphologic findings have been reported by others (*8–10*) who studied virus isolates from cases of variola minor (alastrim) and variola major (true smallpox).

No virus could be isolated from 12 saliva specimens collected from 7 patients and 5 household contacts of patients. Since variola virus may not provoke lesions of the chorioallantois on the first passage, serial passaging as well as two to three reinoculations of the original negative inoculum was done. Also the amount of saliva inoculated was large, 0.1 to 0.2 ml. of undiluted saliva. The failure cannot be attributed to interfering bacterial growth since no sign of such growth was noticed, and the inoculum was always treated with antibiotics before inoculation. Perhaps the amount of virus in the saliva inoculum was not sufficient for isolation, or the failure was due to the fact that plain saliva and not throat washings was used. Incidentally, Downie and co-workers succeeded in isolating variola virus from throat washings during the smallpox exanthem (*11*), and Verlinde and van Tongeren reported isolation of variola virus from the throat of one person with *variola sine eruptione* and from one unvaccinated contact, apparently with asymptomatic infection (*12*).

Antibody Response

Serum samples were obtained 10 to 63 days after onset of illness from 8 of the 10 patients (table 1), and therefore the high frequency of positive test results was to be expected. Four of the eight had no previous successful vaccina-

Smallpox, Alastrim, and Vaccination

Smallpox has come down through recorded history as a dread disease "filling the churchyards with corpses, tormenting with constant fears all whom it had not yet stricken, leaving on those whose lives it had spared the hideous traces of its power, turning the babe into a changeling at which the mother shuddered, and making the eyes and cheeks of the betrothed maiden objects of horror to the lover." Some aspects of this dreary picture that Macauley painted have changed; the use of antibodies has somewhat reduced the degree of scarring, but among those afflicted with classic smallpox, modern medicine has yet provided nothing to significantly improve the prognosis of the smallpox patient. Jennerian vaccination has indeed made the disease much less frequent; it has placed within the power of man the ability to eliminate this disease by eliminating the susceptible population.

The persistence of this disease among the human population is attributable to an unfortunate lack of uniformity in medical thinking, which rests on disagreements on the need for vaccination and on the dangers of vaccination.

Bearing on the first point is the presence of alastrim caused by a virus closely related to that of smallpox but differentiable by appropriate laboratory techniques. Alastrim virus causes a disease in the unvaccinated individual not differentiable from mild classic smallpox, but an outbreak of alastrim is associated with a very low mortality. Further it would appear that epidemiologic factors different from classic smallpox apply to this virus strain, perhaps related to its poorer survival under various conditions.

The absence of secondary cases when a traveler from Brazil exposed many people in Grand Central Station in New York City to alastrim must not be taken to imply that our defensive posture is adequate to prevent an outbreak of variola major should strains of classic smallpox be imported from Asia or some other locus of persistence. Unfortunately the term "smallpox" is generally used to cover both diseases, making it more difficult to convince the reluctant that universal vaccination and revaccination is necessary.

The dangers of vaccination are magnified by a statistical conjury which depends on the paucity of cases of smallpox (which depends on a high state of vaccination), and the complications of vaccination, so rare that they are apparent only when enough vaccinations are performed to keep the disease in abeyance. The experience in the United States, where vaccinia-immune globulin is rapidly available through the American Red Cross, suggests that the significant complications occur in fascinating but exceedingly rare instances of immunological aberration. These are individuals who are kept alive for a longer time in this antibiotic era but whose constitution is incompatible with survival in this "nonsterile" world; the vaccinia virus, deliberately introduced, merely constituting the fortuitous micro-organism (not responsive to known antibiotics) which discloses the immunological aberration.

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tions. Blood was obtained 4 days after illness onset from the other two patients. One of these had been successfully vaccinated 1 year before, which explains the rapid antibody response, while the other, patient No. 5, had never been vaccinated, but the finding of a negative complement fixation titer in blood obtained only 4 days after illness onset is in agreement with published data (*13*).

Patient No. 5, a 6-year-old preschool girl, was tentatively considered to have had *variola sine eruptione* for the following reasons:

1. The child was a frequent visitor to an adjoining house where 11 cases occurred during an interval of 22 days.
2. Onset of illness in the last of these cases occurred the same day as her illness.
3. Variola virus was isolated and identified from skin pocks of 4 of these 11 patients, and blood samples from 5 others showed significant levels of CF antibody without a previous, recent vaccinial or variolous infection.
4. She played, in a yard common to the two houses, with two children from the neighbor-

ing house who were infected, and it is known she had contacts with a third person when these three were in the exanthem stage.

5. She was fully susceptible since she had not previously suffered from variola, had no vaccination scar, had never been vaccinated, and was not vaccinated after these contacts despite repeated advice by the authors who twice saw her in the room where another of the patients in the neighboring house was being nursed.

6. If she had previously been infected by vaccinia or variola virus, one would expect to find significant antibody titers in her serum even 4 days after illness onset, and she had not even detectable HI antibody.

7. She developed fever, headache, and sore throat for 2 days.

8. No further manifestation occurred during a followup of 18 days and occasional examinations in the 2 ensuing months.

9. Her illness could not reasonably be attributed to an etiology other than variola.

10. No evidence has been reported which indicated that infection by variola virus of a fully susceptible individual always provokes an exanthem.

11. Verlinde and van Tongeren (*12*) isolated variola virus from the throat of a woman who had repeated contacts with a confirmed case of variola and did not develop any manifestations, despite having never been vaccinated nor having suffered from variola.

12. If a fully susceptible individual may show no exanthem or no manifestations, it is reasonable to expect that patient No. 5 could develop *variola sine eruptione*, more so if a continuous gradation in the intensity of clinical manifestations of variola is observed when attention is paid to "atypical" clinical pictures (*1*, *14*).

Since the highest titer of CF antibody was found in four cases of *variola sine eruptione* (table 1), it might seem that the milder the clinical type, the higher the antibody response. However, the vaccination history might explain this finding since the four (type 9 according to Dixon's classification) had successfully been vaccinated before, and previously vaccinated persons with variola show a higher and faster antibody response (*13*). On the other hand, only one other patient showed a vaccination scar, and none had previously suffered from variola. The results presented in table 1 are in essential agreement with Downie's findings (*13*).

One serum yielded results deserving comment. The serum from patient No. 8 showed no HI antibody while that fixing complement titrated 1 in 64 (table 1). Since the HI antibody appears earlier and disappears much later than the CF antibody (*13*), this finding is striking. However, it has also been made before (*15*), and Downie and McCarthy found that sometimes there was no correlation between titers of these antibodies (*13*).

The distribution of complement fixation titers (tables 1 and 2) discloses a significant difference between patients and contacts which, incidentally, is to be expected. Serums of 7 of the 10 patients exhibited a titer of 1 in 32 or higher,

Table 1. Antibody response in 10 patients with variola minor, São Paulo, Brazil, 1956

Patient No.	Clinical type of variola [1]	Years after successful vaccination	Date of serum collection (days after onset)	Complement fixation titer	Hemagglutination inhibition titer
1	6	None	26	1:32	1:32
2	6	None	33	1:4	1:128
3	6	None	50	1:8	1:16
4	6	None	63	1:32	1:8
5	[2] 9	None	4	<1:4	<1:4
6	9	1+	4	1:64	1:32
7	6	7+	62	1:32	1:16
8	9	20+	15	1:64	<1:4
9	9	30+	10	1:64	1:64
10	9	40+	16	1:64	1:32

[1] According to Dixon's classification (reference 14): type 6 is "discrete" variola; type 9 is *variola sine eruptione*.
[2] See text for limitations of this diagnosis.

while only 3 of the 37 contacts showed such titers. Besides, when Downie's former criterion of positive titer, a 1 in 5 titer, is used (*13*), 12 of the 37 contacts had a positive complement fixation (table 2) while 9 out of the 10 patients showed a positive titer (table 1). The difference becomes more pronounced if Downie's more recent criterion of positive test result (*16*), a 1 in 10 titer, is accepted.

When the frequency of positive titers is considered, no significant difference between contacts with previous successful vaccination and those unvaccinated is found (table 2). Since the complement-fixing antibody disappears a few months after smallpox or vaccination (*13, 17*), and the previous infection had occurred at least 1 year before, this finding can be interpreted as indicating a limited spread of infection during the epidemic, which fully agrees with other findings (*15*).

Inapparent (Asymptomatic) Infection

According to Downie (*13*), the presence of CF antibodies at titers of 1 in 8 or higher in six persons who had not had clinical manifestations of infection is a definite indication of inapparent infection. This event would be even more probable in donors who are contacts of patients at home and school, such as those in table 2.

Previous vaccinial or variolous infection was exhaustively investigated during the casefinding survey. Two contacts who had no previous vaccination scar or variola showed titers of 1 in 8 and 1 in 64, respectively, while two contacts whose last vaccination scar dated from 14 and 20 years before, respectively, showed CF titers of 1 in 8 and 1 in 16. Thus it seems that these four contacts can be considered as having had inapparent variola, since Downie's detailed studies (*13, 17*) showed that the variolous or vaccinial CF antibody persists less than 1 year. This finding is supported by work in this laboratory (*15*). Besides, two other contacts showing titers of 1 in 64 had their last vaccination 1 and 1½ years before, respectively. This observation can also be interpreted as indicating inapparent infection.

Summary

An epidemic of 54 cases of variola minor in a semi-isolated district of the city of São Paulo, Brazil, in 1956 was investigated during a 3-month casefinding survey. Characteristics of the infection were its limited spread except within households, lack of cases among household contacts who had variola previously, and consistent occurrence of a prodromic period with symptomatology and duration of the period constant.

Variola virus was identified in pock specimens from seven patients, but the virus could not be isolated from saliva specimens of seven patients and five asymptomatic household contacts.

In an antibody survey of 10 patients and 37 contacts, CF antibody titers of 1 in 64 were found in serums of four patients with *variola sine eruptione*; their histories of previously successful vaccinations partly explain this finding. Titers of CF antibody of 1 in 8 or higher found in serums of six contacts indicated inapparent infection, according to Downie's criteria.

Table 2. Distribution of complement fixation titers of 37 contacts of patients with variola minor, São Paulo, Brazil, 1956

Vaccination experience of contacts	Number of donors					
	CF titer <1:4	CF titer 1:4	CF titer 1:8	CF titer 1:16	CF titer 1:32	CF titer 1:64
Successfully vaccinated in the past [1]	12	3	1	1	0	2
Unsuccessfully vaccinated in the past or never vaccinated	13	3	1	0	0	1

[1] Except for one contact successfully vaccinated 1 year before, the previous successful vaccination occurred 1½ to 20 years before.

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Welfare Administration Formed in HEW

The principal welfare programs of the Department of Health, Education, and Welfare were brought together under a new Welfare Administration on January 28, 1963.

The new administration includes the activities of the Children's Bureau, the Bureau of Family Services, and the Cuban Refugee Program, which were transferred from the Social Security Administration. The Special Staff on Aging and the Juvenile Delinquency and Youth Development Staff, which had been reporting directly to the Secretary, were also included.

Dr. Ellen Winston, who was State commissioner of welfare in North Carolina for the past 18 years, was appointed Commissioner of Welfare.

CONGRESS has authorized President Kennedy to designate March 17–23 as National Poison Prevention Week.

Every year 500,000 children accidentally swallow potentially toxic substances, and 500 die. About 90 percent of the reported incidents occur in children under 5 years of age. About half of these children accidentally swallow medicines—aspirin in half of the instances, according to the National Clearinghouse for Poison Control Centers. Cleaning and polishing agents are the poisoning agents in 17 percent of these occasions, and petroleum products, including lighter fluid, kerosene, and some furniture polishes and waxes, in 5 percent.

The danger of bug killers and other poisons marked with skull-and-crossbones cannot be minimized, but the major causes of accidental poisoning in children are ordinary household stores.

Carelessness and ignorance on the part of adults are the main factors in poisoning accidents among children, according to investigators. Many adults tend to underestimate the dangers of household stores and the agility and mobility of small children.

The National Planning Council for National Poison Prevention Week, representing medical and allied professions, industrial and civic organizations, and government agencies, is preparing a campaign to make known the following basic rules for the storage, handling, and disposal of potentially toxic substances in the home:

1. Keep household products and medicines out of the reach and sight of children, preferably in a locked cabinet or closet. Even if you must leave the room for only an instant, remove the substance to a safe spot.

2. Store medicines separately from other household products. Keep all these items in their original containers, never in cups, glasses, or soft-drink bottles.

3. Be sure that all products are properly labeled and read the label before using.

4. Never give or take medicine in the dark.

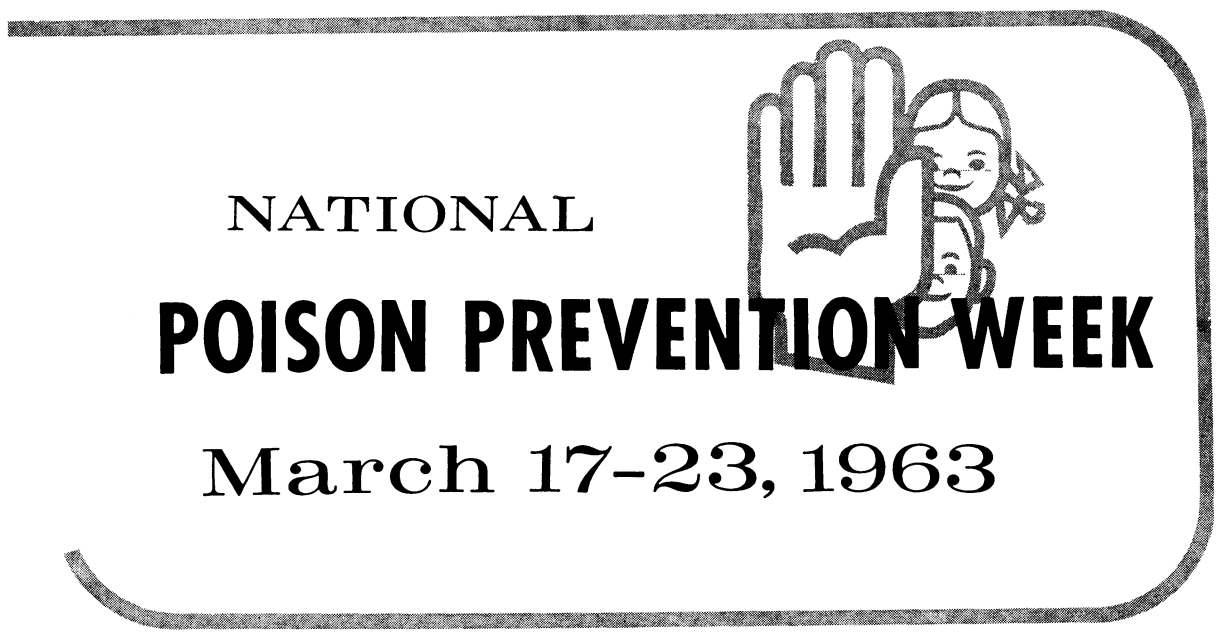
5. Since children tend to imitate adults, avoid taking medications in their presence.

6. Refer to medicines by their proper names. Never call them candies.

7. Clean out medicine cabinets periodically. Get rid of old medicines by flushing them down the drain and rinsing the container with water before discarding it.

In 1962, many States and communities formed committees to organize National Poison Prevention Week activities. These committees represented groups similar to those represented on the National Planning Council. The committees arranged panel discussions and interviews with physicians and pharmacists on television and radio. Speakers' bureaus were established. Open houses and exhibits were held in poison control centers, hospitals, and schools of pharmacy. Pharmacies had window displays and distributed brochures and pamphlets. Posters were distributed and "Clean out the Medicine Cabinet" campaigns were carried on by women's clubs.

To help communities and organizations publicize measures to prevent poisoning accidents, the national council provides a variety of materials, such as fact sheets, news releases, and radio and television material. Brochures, films, posters, and exhibits are available from other sources. A list of materials available from all sources may be obtained from Henry L. Verhulst, Secretary, National Planning Council, National Poison Prevention Week, c/o Division of Accident Prevention, Public Health Service, Washington 25, D.C.



Occupational Health Notes

Organophosphorous Information

Information on occupational disease from organophosphorous pesticides for use by local health officers is being distributed by the California Bureau of Occupational Health.

Publications include a small booklet containing answers to frequent questions and guidelines for medical supervision; information on 2-PAM, particularly in the treatment of poisoning by phosphate ester pesticides; case histories; and a partial listing of laboratories in California prepared to determine blood cholinesterase activity.

Parathion Exposure

During unloading of a trailer in Los Angeles, three employees discovered a ruptured drum of liquid concentrated parathion. The van was closed immediately and the men examined by an industrial physician. Prompt action, stimulated by safety training, prevented excessive exposure. The trailer and cargo were decontaminated by chemical specialists.

X-Ray Exposure

The California Bureaus of Occupational Health and Radiologic Health investigated the illness of a 38-year-old woman who had worked for 12 years as an X-ray technician and was believed to have an occupationally induced blood disease.

In October 1961 she noticed an abrupt onset of fatigue, weakness, muscular aching, nausea, and loss of appetite. Her physician-employer did a routine white count, red count, and blood smear on at least three occasions and found she had a white count of 2,500 with relative lymphocytosis of 90 percent but with an absolute reduction in both lymphocytes and granulocytes. Results of bone marrow biopsies compared with the appearance of peripheral blood, together with her negative history of drug intake and major illness, strongly suggested excessive exposure to ionizing radiation.

The X-ray equipment she used during the previous 5 years exposed the technician in the process of obtaining a radiograph to approximately 1,000 mr./hr. When she held a patient during an exposure, she was in a field of about 20,000 mr./hr. She was frequently in the room during fluoroscopy without protection of a leaded apron. The direct beam overlapped the lead glass fluoroscopic screen by 2 inches on either side.

The technician received most of her exposure, estimated at a monthly total of about 12,000 mr., during fluoroscopic examinations. (Maximum permissible dose recommended is 100 mr./wk. or 400 mr./mo.) At no time during the last 5 years did she carry a dosimeter or wear a film badge to monitor her exposure.

Radioactive Well-Logging

Beginning with radioactive well-logging field stations, the Oklahoma State Department of Health has launched a comprehensive industrial inspection program.

Inspections cover operating, handling, and safety procedures, personnel monitoring, labeling and posting, and storage facilities. Comparing instructions in company operations manuals with field practices has shown that sources, trucks, and storage containers are seldom labeled for radioactivity, and exposure levels outside controlled areas are frequently 10 to 20 times higher than the 2 mr. per hour set forth in the AEC regulations or in the company manual.

At one site, throughout the shop, investigators found sources of radium (25 mg.) and radium-beryllium (400 mg.) unlabeled. A neutron logging tool containing 400 mg. of Ra-Be had a surface intensity exceeding 3,000 mr./hr. The truck used to transport logging sources to the field was not labeled and provided no shielding from the gamma and neutron radiation of the tool. Exposure levels determined with an ion chamber survey meter along the side panel of the truck exceeded 2,000 mr./hr.

Lead Concentrations

A survey of a secondary lead-smelting plant in Pennsylvania indicated that lead concentrations in the air exceeded the threshold limit value by 100 to 170 times. The plant was ordered to introduce controls.