ous system comes to us from the cerebral process, which is induced through sense organs. On the other hand we receive through the resolving power of receptive systems information about the environmental source of stimulation. In visual perceptions derived from both eyes, for example, paralactic shift is utilized in composing an integrated stereo image. The impression that the sensory stimulation originates in the environment is confirmed through the directed motor reaction—for example, through the grasping of a visually localized object. The successful attempt to grasp the object confirms the correlation between perception and reality. Involved are consistent temporal and spatial relationships which produce the impression of causality (*19*).

Simple mechanisms for the preservation of life are genetically controlled and subject to phylogenetic selection. Important individual behavioral patterns are determined prenatally. Complex reactions, on the other hand, are learned postnatally, and their release is under the control of conscious will. Through frequent repetition, psychic functions become partially or totally automated. As a result, the desired success is achieved with more speed and more precision, and mechanisms of great complexity are mastered.

Summary

This article is based upon data which are suitable for the correlation of behavioral research and experimental neurophysiology. Causal thinking manifests a sort of integrative activity which brings simultaneous and successive patterns of nervous excitation into a subjectively meaningful frame of reference. While neuronal patterns determine the content of consciousness, they fail to provide clues concerning the transformation of such patterns into subjective experience.

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Arbovirus Infections of Laboratory Workers

Extent of problem emphasizes the need for more effective measures to reduce hazards.

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Prior to 1950, only an occasional report was concerned with the need for protection of laboratory personnel who came in daily contact with disease-producing agents. Sulkin and Pike (*1*) had collected data on viral infections contracted in laboratories in the hope that this information would be helpful in determining where the greatest caution must be exercised in working with viruses. The magnitude of the overall problem of laboratory-acquired infections, however, became evident in an extensive survey (*2*) which revealed over 1500 instances of laboratory-acquired infections resulting in 39 deaths. A standing Committee on Laboratory Infections and Accidents of the American Public Health Association (APHA/CLIA) (*3*) has maintained a file of cases of laboratory-acquired infections whether reported to the public or by private communication; so far, there have been over 2700 cases with 107 fatalities.

Molecular biologists interested in the relation of viruses to the metabolic systems of cells and in the structure of their nucleic acids may now be added to the many virologists who have long worked with a heterogeneous group of viruses known as arboviruses. The health hazard inherent in the manipulation of these viruses may not be well known to many of the newer investigators who lack clinically oriented training.

The arboviruses, a contraction of

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"arthropod-borne viruses," are so named because they are transmitted biologically by arthropods between vertebrate hosts. Of more than 200 viruses now classified as arboviruses, approximately 50 have been associated with disease in man, and many have caused overt laboratory infections. This high incidence may have resulted from the marked acceleration of studies of this group of viruses and from the increase in the number of persons who handle these agents.

This article, based on data from laboratories in 38 countries (*4*), reveals risks for those who work with arboviruses. The information obtained was related to the earlier records of the American Public Health Association Committee on Laboratory Infections and Accidents. We now report on the extent of the problem of accidental infection, without regard to recommended measures or devices, since guidelines for laboratory safety and references to specific procedures have been reported (*5*, *6*).

Laboratory groups working with the arboviruses were asked to provide information concerning: (i) the number and nature of overt laboratory-acquired arbovirus infections by virus type, (ii) the circumstances that led to infection, (iii) practices in laboratories that may relate to detection and prevention of infections, and (iv) the number of people at risk.

Laboratories responding to the questionnaire ranged from 29 with less than five individuals employed to 13 with more than 15 persons on the staff. Over half of the 91 laboratories surveyed had five to 14 employees.

Of 428 overt laboratory-acquired infections due to arboviruses, 16 were fatal (Table 1). Information on 129 cases first became available through the recent survey. Of the 192 arboviruses currently registered in a catalog prepared by the American Committee on Arthropod-borne Viruses (*7*), 36 are reported to have caused illness acquired in the laboratory, and at least 14 induced illnesses of such severity that need for extreme precaution in laboratory manipulation was indicated (*6*). Most of the arboviruses known to have caused laboratory-acquired infections are in group B. The data do not necessarily reflect the risk of infection from each of the viruses listed because some cases tend to be concentrated in a single area or even in a single laboratory, some viruses are seldom used, and others are used in many laboratories. For example, 24 cases of Venezuelan equine encephalitis were the result of a single accident (*8*), and most of the cases of Kyasanur Forest disease virus infection occurred in two laboratories (*9*). Seven cases of vesicular stomatitus virus infection were reported by one institution (*10*), and all the infections from Colorado tick-fever virus occurred in a single laboratory (*11*). The viruses causing these infections may eventually be classified (for administrative purposes) according to their various propensities for causing laboratory infections. Many caused overt disease of such severity that hospitalization for periods of 2 days to 3 months was required; seven different viruses caused death. Although Kyasanur Forest disease virus has not been reported to be fatal for any laboratory personnel, it is highly infectious. Clinically apparent infections occurred in 65 laboratory workers, principally in India, New York, and Washington.

In several instances, an arbovirus was first found to be capable of producing disease in man as a result of infection of laboratory personnel. Six persons with laboratory-acquired disease due to louping-ill virus were the only known human cases until two instances of naturally acquired disease were reported in 1948 (*12*), and the first recorded case of Zika virus infection in man was a laboratory-acquired

Table 1. Overt laboratory-acquired infections with arboviruses. APHA/CLIA, American Public Health Association, Laboratory Section/Committee on Laboratory Infections and Accidents. ACAV/SLI, American Committee on Arthropod-borne Viruses/Subcommittee on Laboratory Infections. Numbers in parentheses represent cases for which information first became available through recent ACAV questionnaire.

Arboviruses	Information from		Total cases	Deaths
	APHA/CLIA	ACAV/SLI		
Group A				
Chikungunya	13	13 (6)	19	
Eastern equine encephalitis	2		2	
Mayaro	1	3 (2)	3	
Mucambo	2	2	2	
Venezuelan equine encephalitis	92	46 (26)	118	1
Western equine encephalitis	5		5	2
Group B				
Dengue	4	4 (2)	6	
Japanese B encephalitis	1	1	1	
Kunjin	2	1	2	
Kyasanur Forest disease	9	60 (56)	65	
Louping-ill	19	3 (2)	21	
Omsk hemorrhagic fever	2	1 (1)	3	
Powassan	1	1	1	
U.S. bat (Rio Bravo)	5	5	5	
St. Louis encephalitis	1		1	
Spondweni	2		2	
Tick-borne encephalitis	8	13 (10)	18	2
Wesselsbron	2	2 (2)	4	
West Nile	3	11 (8)	11	
Yellow fever	37	1 (1)	38	8
Zika	1		1	
Group C				
Apeu	1	1	1	
Marituba		1 (1)	1	
Oriboca		1 (1)	1	
Bunyamwera				
Bunyamwera	4		4	
Germiston	3		3	
Simbu				
Oropouche		2 (2)	2	
Tacaribe				
Junin	2	3 (3)	5	1
Machupo	1	1	1	1
Vesicular stomatitis virus				
Vesticular stomatitis	38	1	38	
Ungrouped				
Colorado tick fever	7	6 (1)	8	
Nairobi sheep disease	1		1	
Piry	1	3 (3)	4	
Rift Valley fever	28	1 (1)	29	1
18 AR 1742 (unidentified)		1 (1)	1	
AR 1792 (unidentified)	1		1	

Table 2. Comparison of number of reported infections with number of viruses handled by laboratories. Numbers in parentheses represent total number of laboratories checked.

Viruses handled (No.)	Laboratories reporting cases		Cases (No.)
	No.	Percent	
1–5	9 (31)	29	16
6–10	6 (14)	43	19
11–20	8 (20)	40	32
21–30	7 (11)	64	42
31–40	4 (6)	67	9
41	6 (6)	100	23
Unknown	1 (3)	33	1

infection (*13*). Several additional arboviruses (Germiston, Kunjin, Piry, and Nairobi sheep disease) are not known to cause disease in man through naturally acquired infection, but yet they have produced infections in the laboratory.

Acquisition of laboratory infections is not always similar to transmission of the disease when it occurs naturally. For example, none of the cases of encephalitis was believed to be transmitted by an arthropod, and only one case of yellow fever was thought to be due to the bite of an infected mosquito. Many persons have become infected while working with dried virus preparations which provide ideal circumstances for aerosol transmission. A case of St. Louis encephalitis and a fatal case of Russian spring-summer encephalitis apparently resulted from aerosol transmission of such materials (*14, 15*). Contaminated dust from mouse cages was apparently responsible for several infections with the virus of Venezuelan equine encephalomyelitis (*16*) and for a fatal infection with Machupo virus; thus, these infections were probably also acquired by the respiratory route.

Table 3. Proved or probable sources of laboratory-acquired arbovirus infections. Cases are distributed according to the one most probable source.

Probable source	Infections (No.)	Percentage of total
Experimentally infected animals	93	21.7
Not indicated	84	19.6
Aerosol	74	17.3
Agent handled	70	16.4
Accidents	43	10.0
Preparation of vaccines, antigens, and other	35	8.2
Experimentally infected chick embryos	9	2.1
Discarded glassware	9	2.1
Autopsy (including known accidents)	8	1.9
Clinical specimens	3	0.7

Although many pathogens decrease in their virulence for the natural host after several passages, a number of overt infections have been acquired in the laboratory by individuals working with "laboratory-adapted" strains of various arboviruses; hence, virus strains that have been passed through animals many times may be still pathogenic for man (*14, 17*). A serious laboratory infection with St. Louis encephalitis virus occurred in an investigator who had worked with a strain that had been passed through mice many times over a period of 16 years. Disease occurred in an individual who had worked with a strain of Rift Valley fever virus that had undergone over 150 mouse passages, and Japanese B encephalitis occurred in an individual who had worked with a strain that had been through six passages in a mouse brain and one passage in chick-embryo cell cultures.

The intensity of activity of the reporting laboratories may be indicated by the number of viruses with which they had been working (Table 2). The percentage of laboratories reporting infections increased directly with the number of viruses being studied in the laboratory. This was the only apparent relation between a characteristic of the laboratory (size of staff, length of operation, and number of viruses handled) listed on the questionnaire and number of infections (including subclinical) reported.

Failure of the size of staff to be directly related to the number of acquired infections may be due to the increase in the proportion of supportive personnel in such laboratories—individuals who have less exposure to infection. Unless the maintenance of records of acquired infection is an administrative routine of the laboratory and unless surveillance has been unchanging, one would not expect a retrospective query to obtain as many early as later cases of infection. The lack of relationship between number of infections and length of operation of laboratories may be ascribed in part to an inadequacy of reporting and in part to changing methodologies. Because of these variables, a man-year exposure index was not presented for any virus.

Over 80 percent of the currently classified arboviruses have been recognized since 1950. The steady increase

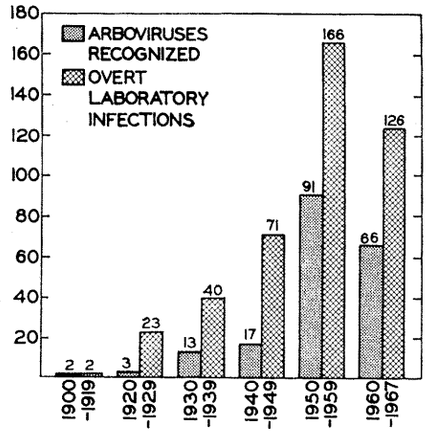

Fig. 1. Number of overt laboratory infections and recognition of new arboviruses by decade. In addition, 12 arboviruses have been added to the ACAV catalog; one virus, Canjam, was responsible for an overt mild febrile illness.

in the number of overt infections acquired in the laboratory correlates with the increase in the recognition of new arboviruses (Fig. 1). Changes in the kinds of agents involved in laboratory infections and in the circumstances resulting in infection to some extent reflect trends in areas of research and interest in certain agents (*18*). Prior to 1950, bacterial infections accounted for over one-half of known overt cases of laboratory-acquired infections, while viruses were responsible for about 20 percent of the total. Since 1950, there has been an increasing number of laboratory-acquired infections due to viruses, with more than half due to arboviruses. This is probably the result of the marked acceleration in research and diagnosis in connection with arboviruses and a consequent increase in the number of persons and laboratories handling such agents. A large proportion of the total number of infections due to arboviruses occurred since 1950 (Fig. 1). Relatively few laboratories worked with these viruses prior to 1941, and the agents causing laboratory infections at that time reflect the area of interest prevailing then.

The exact source of a laboratory-acquired infection is frequently obscure. Often it is known only that an individual had been working with a particular agent or that he had been in contact with infected animals. In other situations, it is known that the atmosphere of the laboratory had become contaminated. That an aerosol may be unwittingly produced by a variety of common laboratory procedures has been convincingly demon-

strated (*19*). The potential source of infection has been more fully appreciated since the use of atmospheric sampling devices which show that such common and simple procedures as removing stoppers, expelling the last drop from a pipette, or removing plugs from a tube may produce aerosols near the laboratory bench (*20*). Filtration of infectious material may result in contamination of a vacuum line or pump unless adequate precautions are taken, and maceration of infected tissue by a variety of means may produce an infectious aerosol. Blenders for mechanical disruption of infected tissue have been designed to minimize the chance of leakage and to provide a means of drawing off fluid without removing the top (*21*). If, in addition, the operation is performed in a sterile chamber with a plastic cover over the apparatus, there should be little hazard. The opening of sealed glass ampules containing lyophilized active viral material constitutes a serious inhalation hazard in the laboratory. Special techniques have been recommended for opening such ampules.

Sources of laboratory-acquired arbovirus infections are shown in Table 3. In many instances, it was known only that the individuals had been working with the agent and that the source was probably aerosol inhalation. In addition to those classified as due to an aerosol, a number of infections under other headings were probably transmitted by aerosols. Known accidents resulting from situations that could have been avoided accounted for about 10 percent of the total.

The survey of laboratory-acquired infections has provided information concerning the number of cases and the identity of viruses that cause infections. Regular reporting of laboratory-acquired infections to the American Arbovirus Committee or American Public Health Association would stimulate the development of more effective measures to reduce the hazards in arbovirus laboratories. Regular testing of all members of the laboratory staff for antibodies to all viruses that they handle should be encouraged as a means of assessing the effectiveness of safety procedures. The greatest hope of preventing laboratory-acquired illness lies in the recognition of the sources of infection; the unrecognized sources constitute the greatest problem.

While there is no evidence that use of immunizing substances such as serum from convalescents or specific immunoglobulin is of any value after symptoms of arbovirus infection appear, a rationale based on studies in experimental animals has been developed for use of such substances for passive immunization immediately or soon after accidental exposure. Because of the numbers of laboratory workers required to handle an increasing number of arboviruses in diagnostic and research studies, efforts are being made by the National Communicable Disease Center and the World Health Organization to collect, pool, and accumulate serums of convalescents from specific arbovirus infections. These serums are being processed into specific immunoglobulins and will eventually be available on a restricted basis for use after certain types of laboratory accidents.

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NEWS AND COMMENT

Federal Research Funds: Science Gets Caught in a Budget Squeeze

As the first session of the 90th Congress draws to a close, it is clear that President Johnson's legislative program has been badly gutted. A number of factors—the rising economic and emotional costs of the Vietnam war, a general fiscal squeeze, poor Democratic congressional leadership, a stronger conservative coalition, and growing antipathy between the legislative and executive branches—combined to produce a Congress this year that ignored or drastically altered many of the President's legislative requests. The closing months in particular have been marked by an economy wave that engulfed virtually all non-war-related spending requests, from foreign aid to urban rejuvenation. In the scramble to save another nickel, few targets proved more tempting than federal support of research and development. As Representative Frank T. Bow (R–Ohio) expressed it: "R & D spending is a prime area for economy."

Such attitudes made it certain that the budget and appropriations process for fiscal year 1968 would provide no bonanza for science. Thus there are probably two main points to be made in any analysis of how science fared this year: One is that science received rougher-than-usual treatment at the hands of congressional appropriations committees—though things could have been worse; the other is that things are certain to get worse, thanks to the latest budget-cutting scheme announced