INFECTIOUS DISEASES

ANNUAL REVIEW OF SIGNIFICANT PUBLICATIONS

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VIRUSES and viral diseases were the subjects of continued intensive study in the past year. Attempts to prepare vaccines for the prevention of specific infections, especially of the respiratory tract, have not had much success because of the complexities involved. No important curative agents were discovered, nor has a causal relation of viruses to cancer in man been proved. Many new antimicrobial agents, or old ones with new names, were tested. As causes of disease and death, gram negative bacillary infections now displace those formerly caused by gram positive cocci, as a result of iatrogenic impairment of host-resistance and other factors. The incidence of venereal diseases and of tuberculosis increased. Meningococcal meningitis, the one disease for which antimicrobial prophylaxis seemed to have the most value, caused serious epidemics despite efforts to control it.

Antimicrobics

New Antimicrobics. According to Garrod, there is little to be gained by the increasingly unprofitable search for new antimicrobics from natural sources. Some of the recently advertised ones are the same as, or similar to, ones in use¹. Synthetic or semisynthetic ones may hold more promise.

Two new broad spectrum antimicrobics especially for the control of gram negative bacillary infections were discussed in three papers in the Journal of the American Medical Association of September 14th, 1964. Gentamycin is active against *Pseudomonas*, less so against *Proteus* and *Staphylococcus*. It resembles streptomycin, neomycin, kanamycin and paromomycin chemically, its antibacterial action is about the same and it occasionally causes deafness^{2a}. Cephalothin (Keflin), a semisynthetic broad spectrum agent has a similar range of action and is less toxic even in patients with renal failure. It was ineffective against *Pseudomonas* and enterococci. It differs

chemically from penicillin and can be used against penicillin-resistant staphylococci, and for patients sensitive to penicillin. It is not absorbed when given orally. Neutropenia may be induced².

Sodium colistimethate (Coly-mycin) 2 to 2.5 mg./kg. every 12 hours injected intravenously cured five of eight patients infected with *Pseudomonas*. Smaller dosage was necessary when the renal function was impaired. It may be neurotoxic, cause apnea and must be used with caution in the presence of chronic debilitating disease, renal impairment, hypoxic states, and if muscle relaxants, corticosteroids, narcotics or sedatives are given at the same time⁴.

The activity of nafcillin, ancillin, and cloxacillin was reduced in media containing serum, but cephalosporin was unaffected³. Several observers found no differences in the results of therapy with ampicillin, nafcillin, oxacillin, methicillin and cephalothin. The action of lincomycin and pristinomycin was said to be similar to that of streptogramin, streptogramin, spectinomycin, synergistin and mikamycin^{6,7}. An antagonism between lincomycin and erythromycin interfered with their effect on staphylococci⁸. Lyme cycline was said to be as effective as tetracycline for treating chronic bronchitis. Hamycin was active against *Cryptococcus neoformans* and *H. capsulatum* in inoculated mice¹⁰. Ethambutol may be effective against tubercle bacilli refractory to other agents¹¹. Several years must pass before the value of any of these agents can be judged. As if the names for new products mentioned so far are not confusing enough, these also have been coined: quinacillin, everinomycin, almaricetin, pediamycin, viractin, monicamycin, enteromycin, seligomycin, xanthomycin, rubiflavin, antimycin, oligomycin, tolfanate and others¹². There is no limit for new alphabetic combinations.

Antimicrobial Therapy. The administration of huge amounts of antimicrobics given "just to be sure" is deprecated. But recent studies showed that penicillin in doses of 20 to 60

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million units (12 to 36 grams) a day given intravenously cured many gram negative bacillary infections. The amount in the serum reached 737 units/ml. Cerebral irritation occurred in patients with renal failure or central neural disease. Obviously, the sensitivity of gram negative bacilli to penicillin should be determined. Those inhibited by 78 units/ml. or less are classed as sensitive; resistant ones resist 625 units/ml. and are uncontrollable¹³.

Thirteen patients with bacterial endocarditis were treated successfully with propicillin (phenoxypenicillin) or ampicillin given orally. Infections with *Str. viridans* responded better than those caused by *Str. fecalis*¹⁴. Penicillin given prophylactically during cardiac catheterization had no influence on the incidence of subsequent bacteremia. Its use therefore is unwarranted¹⁵.

The therapeutic effect of penicillin combined with sulfonamides is unpredictable. Increased, indifferent or decreased antimicrobial effect may follow. If the combination is used, full doses of each are indicated. Semisynthetic penicillin alone or combined with penicillin G and other antimicrobics was said to be of therapeutic value against infection with isoniazid-resistant tubercle bacilli¹⁷.

Acute pericarditis occurred as a hypersensitive reaction to penicillin¹⁸, and oxacillin caused hepatitis¹⁹. Huge doses of penicillin caused severe anemia in two patients²⁰. Pencilloyl-polylysine introduced as an agent to detect sensitivity to penicillin, itself caused a generalized eruption after the injection of a skin-test dose²¹.

Airborne contamination with penicillin of many products made in large pharmaceutical plants is a serious problem. It would be difficult to recall such products now on the market and to destroy the ones in reserve.

Chloramphenicol suppressed the formation of antibodies *in vitro* and in experimental animals. Therapeutic doses in eight patients suppressed antibody formation after the injection of tetanus toxoid in six and was hemotoxic in four²². Chloramphenicol applied to the conjunctiva caused pancytopenia in a patient whose niece had succumbed to aplastic anemia after oral therapy²³. The reason for the topical use of the agent is unclear.

Amphotericin B should be used only when actually needed. The blood urea was increased in amount in 93% of 81 patients during treatment. The renal function was persistently reduced in 7 of 16 patients who received more than 4 g., and in six of 36 who were given less. Tubular lesions and deposits of calcium

occasionally were found. Other untoward effects also occur. The subject was discussed in two papers in the *Annals of Internal Medicine* of August, 1964. Actinomycin D was teratogenic in rats^{23a}.

Broad spectrum antimicrobics decrease the rate at which colon bacilli are killed by human serum, probably by inhibiting bacterial metabolism and impairing the lytic action of serum. The matter may be of therapeutic import²⁴. The same amount of antimicrobics entered the blood after intraperitoneal injection as from injection by other parenteral routes. The method may be used in place of intravenous and intramuscular injection²⁵.

In regard to indiscriminate antimicrobial therapy, Harris wrote that something has weakened clinical judgment: physicians who prescribe digitalis or quinidine (which are poisons) with the utmost caution, pounce avidly on chloramphenicol and other antimicrobics for minor illnesses. They would always make tests of sensitivity before injecting tetanus antitoxin, but not before giving penicillin whose danger in causing a reaction is as great²⁶. Antimicrobial-induced diseases were described in a book²⁷.

Viral Infections

Respiratory Tract Infections. Sir Christopher Andrewes, who with Smith and Laidlaw, discovered the virus of influenza in 1933, has also contributed to the knowledge of common colds. In a review, he points out the complex, poorly understood epidemiology of these ubiquitous infections. Respiratory tract viruses no doubt spread from person to person by the airborne route, but various determinant factors operate to cause epidemics. Meteorologic changes seem to be important at times, but a wide range of stresses, including chilling, may disturb the host-parasite relationship enough to permit the invasion of microbes. The operation of viral interference and of interferon itself probably play a role²⁸. By indirect methods, droplets bearing the viruses were expelled in greatest amount by sneezing. Most of them fell to the ground and about 10% were small enough to be airborne. Saliva contained very little virus. Viruses die soon after shedding²⁹. Four papers on airborne infections pertaining especially to those acquired in laboratories and in hospitals appeared in the October, 1964, *American Journal of Public Health*. Methods for their control were outlined.

Rhinoviruses. Fifty-three types of rhinovirus are known and there are many others. Rhinoviruses of 46 types were isolated from 10% of infected adults and from 5% of children. Children were more severely affected, and half

of them had viral pneumonia³⁰. Adult volunteers inoculated with rhinovirus usually had coryza, but several had tracheobronchitis³¹. The multiplicity of specific types and the constant changes in the human population explain why some persons have repeated colds in a season. Little hope was held for the preparation of effective vaccines³². Hilleman discussed the problem of vaccination against a variety of viral infections³³. Perhaps the introduction orally of viruses into the enteric tract in specially coated containers may elicit immunity without causing respiratory tract symptoms or illness. Epidemiologic and antimicrobial prophylactic efforts have failed as preventive measures.

Adenoviruses. Adenovirus Types 4 and 7 caused sharp, localized, winter epidemics among military personnel over a 4-year period³⁴. The antibody titer for adenovirus rose in several victims of respiratory tract infection and acute thyroiditis suggesting that the virus was the cause of both. Pharyngitis, cough and fever often accompany epidemics of keratoconjunctivitis caused by Type 8 virus each summer in Taiwan³⁵.

Apprehension was raised lest contamination with an oncogenic hybrid offspring of a mating between adenovirus Type 7 and SV40 virus used in vaccine may occur. This raises the further question whether vaccination against usually mild infections is desirable or necessary. The distribution of adenovirus 7 vaccine has been stopped for the time being.

RS Virus. Respiratory syncytial virus caused two winter epidemics in a nursery for premature infants. Coryza usually lasted one to eight days before respiratory distress began³⁷. Pneumonias occurred in 9 of 14 sick infants. RS Virus caused 60% of pneumonias among infants and children in Newcastle³⁸. Antibody against the virus was present in 66% of 329 persons, chiefly in adults³⁹. Neutralizing antibody was found in 25% of persons of all ages, and after four seasons, the percentage rose to 83⁴⁰. RS virus is related to measles virus and may cause an exanthem.

Reovirus caused hepatitis, encephalitis, myocarditis and pneumonia in children. In one victim, virus was recovered from the brain and feces⁴¹.

ECHO virus Type 25 is an enterovirus, and a strain isolated from feces caused febrile respiratory tract infections in intranasally inoculated adult volunteers⁴².

Influenza. A commercially prepared polyvalent vaccine that contained antigens to the

current viruses failed to prevent infection among 90 children against influenza A as compared with 90 control subjects. Antibody induced in the blood in titer higher than 1:64 was not protective⁴³. Oil-adjuvant vaccine was shown to evoke antibody that persisted as long as 16 months⁴⁴, but in accordance with the preceding sentence, the protective value of measurable antibody in the blood is of little significance. In another institution, an outbreak of influenza A2 affected children who had been vaccinated with a polyvalent vaccine five months before. The number of illnesses among the vaccinees was slightly less than in nonimmunized children⁴⁵. Encephalopathy appeared 12 hours after a child had received a polyvalent vaccine⁴⁶.

U.S. Public Health Service officials predicted no widespread epidemics of influenza this year. From past experience, one wonders how trustworthy such predictions are. Influenza A2 was rampant in the United States and in Europe in the winter of 1964-1965⁴⁷.

By a specific immunofluorescent technique influenza virus was detected in bronchial epithelium 8 hours after the inoculation of mice, mostly in the cytoplasm and occasionally intranuclearly. Virus reached a maximum amount in tissue in two to three days and progressively invaded the bronchi, bronchioles, alveolar ducts and alveoli. Fluorescence vanished after seven days⁴⁸.

A parainfluenza virus liberated a pyrogen from granulocytes in the blood that caused the fever of infection⁴⁹. A lysozymic or antibody like microbic-inhibiting substance was demonstrated in mucosal secretion years ago by Fleming. Recent studies of nasal secretion disclosed that its viral neutralizing activity correlated with the presence of specific antibody to each of several viruses tested. During respiratory tract infection, antiviral substance was chiefly in the gamma 2-globulins⁵⁰.

From 210 students with acute respiratory tract infections, only two kinds of viruses were recovered. In 122, serologic evidence of influenza B was present in 16 and of respiratory syncytial virus in five⁵¹. To account for the large percentage of unidentified infections, either the technique used was faulty, immune bodies failed to appear, or unknown microbes awaited discovery.

Study of 300 other students with acute pharyngitis-tonsillitis disclosed hemolytic streptococci to be the cause in about 25%, as recorded in previous surveys. Viruses were causal in 38%, and 36% were of undetermined

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origin. Surprisingly, the virus of herpes simplex was implicated in 13%. Coxsackie, influenza, parainfluenza and adenoviruses accounted for three to five per cent of infections. Twenty-three of 86 patients, regarded as having a viral infection also harbored hemolytic streptococci. Specific diagnosis of the six different infections mentioned seldom could be made clinically because of many features in common. A few points of differentiation were helpful: Exudate, cervical adenitis and leukocytosis were present in 26% of streptococcal infections and in 14% of the others. General aching was present in 3.4% of patients with streptococcosis, as compared with 23% during viral infections. Penicillin therapy failed to shorten the course of any of the infections and broad spectrum agents seemed to prolong illness. Penicillin is indicated: (1) if the patient has had rheumatic fever, glomerulonephritis or repeated attacks of streptococcal sore throat, (2) in the presence of exudate, severe inflammation, otitis media or leukocytosis higher than 13,000/u. mm., (3) for severe sore throat in the absence of rhinorrhea, hoarseness or cough, and (4) if other chronic disease exists. Cultures of the exudate and other tests to identify the cause should be made in any event⁵².

Pneumonias. Specific pneumonia occurs in one-third of victims of varicella, but in less than 3% of those with herpes zoster. Twenty-two cases of the latter were reviewed⁵³.

Mycoplasma Pneumoniae. Two reports emphasize the frequency of respiratory tract infections caused by *Myco. pneumoniae*, with and without pneumonia^{54, 55}. One paper perpetuates the outmoded term "primary atypical pneumonia" that should not have been coined in the first place. *Myco. pneumoniae* infections are nonseasonal, but they accompanied a winter epidemic of adenoviral pneumonia⁵⁴. These are circumstances that I described in 1938 before either agent was known. An agent was recovered that in retrospect probably was *Myco. pneumoniae*. The historic aspects of these earliest observations were recited⁵⁶.

Cold agglutination occurred in eight patients who had meningoencephalitis and mild upper respiratory symptom without pneumonia. Two had mucocutaneous fever (Stevens-Johnson syndrome)⁵⁷. In 1944, I reported severe non-pneumonic disease in a patient whose cold-agglutination titer rose to 1:20,000⁵⁸. During the course of infection, *Myco. pneumoniae* causes cold-agglutination of erythrocytes by altering the I antigen that evokes erythrocytic auto-antibody⁵⁹.

A hemagglutination test for the detection of antibody for *Mycoplasma pneumoniae* is simpler to perform than the immunofluorescent procedure⁶⁰. Antibody against the microbe was demonstrated in titer of 1:256 or higher in five victims of mucocutaneous fever (Stevens-Johnson syndrome), a disease often characterized by a viral-like pneumonia⁶¹. Because *Mycoplasma* (PPLO) has no rigid cell wall, it is pleomorphic and hard to see microscopically. Question was raised if it is a virus, a fungus, or a bacterium that has lost its wall and therefore is not an independent microbe⁶². A newly recognized *Mycoplasma* caused fatal septicemic disease in puppies⁶³.

Psittacosis caused 24 cases of pneumonia in Scotland from 1950 to 1963. Several victims contracted the infection from pigeons or budgerigars. In 1963, 54% of pigeons in Glasgow were found to be infected, but apparently they were not a source of disease in man⁶⁴. Antimicrobics added to food for parakeets and other birds was said to minimize the risk of spreading psittacosis⁶⁵.

A peculiar form of pneumonia occurred in six patients who had renal transplants and were treated with azothioprime and prednisone as immunosuppressants. Cold agglutination of erythrocytes occurred in five. The disease, uninfluenced by antimicrobics, lasted 12 to 34 days. Necropsy in one disclosed *Pneumocystis carinii* and cytomegalic inclusion disease⁶⁶. Others may have been caused by *Mycoplasma*.

Cytomegalovirus was recovered post mortem from the lungs of four recipients of renal homografts⁶⁷. The disorders represent maladies induced by iatrogenically impaired resistance. The virus was found in 1% of 200 well children. Among 20 symptomless virus-positive children, 14 had hepatomegaly, and five had splenomegaly. The virus was isolated from nine of 23 children with chronic hepatic disease^{67a}.

Other Viral Infections

Rubella. Rubella, absent for 22 years, caused a large epidemic in Alaska as described in two papers in the J.A.M.A. of February 22nd, 1965. Virus was recovered 13 days before the rash appeared and for 6 days afterward. Inapparent and mild infections were common, and 40% of patients had no rash. Rubella virus isolated from seven patients during an epidemic in Texas was pleomorphic by electronmicroscopy. Some victims had classic rubella, others had severe arthritis. Clinical differentiation from ECHO virus infection may be impossible and the name rubecho disease was applied to an outbreak in Africa. Nine months later more

than 30 infants were born with congenital defects⁶⁸.

Rubella virus was isolated up to 4½ weeks after birth from three malformed infants whose mothers had been infected in first trimester⁶⁹. Virus survived in *utero* in mothers for at least 36 weeks⁷⁰. Four nurses contracted rubella by handling congenitally infected infants some of whom shed virus for months after birth^{70a}. During an epidemic, the injection of gammaglobulin seemed to prevent rubella as compared with control persons⁷¹. In other studies, gammaglobulin failed to prevent rubella in mothers and in experimentally infected children⁷². For the present, it may be wise not to rely on gammaglobulin as a protective agent. About 17% of pregnant women have no demonstrable antibody for rubella⁷³. The salivary gland virus caused 1% to 3% of birth defects. Unfortunately, the infection usually is inapparent in adults and is undetectable without special investigation⁷⁴.

Measles. In a region of Alaska where measles had not occurred since 1942, 164 persons received live measles vaccine and gammaglobulin. About 7% of them reacted with fever and 6% had a rash. The failure of antibody to increase in titer in seroimmune persons indicated that durable immunity had followed a natural attack of the disease⁷⁵. The immunity evoked by one injection of an improved vaccine persisted for 30 months. Reactions thereto occurred in 5% of vaccinated children⁷⁶.

At a symposium on virology in Florida, Smorodintzev reported success in vaccination against mumps with live attenuated virus applied transnasally. The vaccine can be administered with antimeasles vaccine, but not with gammaglobulin which neutralizes mumps virus.

Contrary to previous opinion, the incubation period of infectious mononucleosis instead of being four to 15 days was 34 to 39 days in seven patients⁷⁷. At a recent meeting of the American Association for the Advancement of Science, Schneider described evidence that a virus caused the disease. The agent was said to have been isolated in tissue cultures from the blood and from the liver of patients. A benign infection resembling infectious mononucleosis, presumably viral in origin, was transmitted to nine patients by the transfusion of blood after open cardiac surgery. Symptoms appeared after three or four weeks⁷⁸.

Herpes Simplex. Constitutional symptoms and dermal lesions among five wrestlers posed

a diagnostic problem, until it was shown that close contact and dermal abrasions favored infection with herpes simplex virus as "Herpes gladiatorum"⁷⁹.

Fatal herpes simplex necrotizing pneumonia of an infant was acquired during passage through the birth canal of the mother with primary herpetic vulvovaginitis. Gammaglobulin injected into the mother before delivery had no effect⁸⁰. Herpes simplex cervicitis was caused by sexual contact with recurrent herpetic penile lesions⁸¹. Herpes viral pneumonia and toxoplasmic encephalitis were fatal in a patient with Hodgkin's disease treated with prednisone, alkylating agents and roentgen rays. Herpes virus is an occasional unsuspected cause of viral pneumonia⁸². Herpes simplex in a 9-year-old boy was said to have caused 17 episodes of psychosis during three years, coincident with vesicles on the oral mucosa and encephalitis⁸³.

Viral Hepatitis. Among 737 military men exposed to hepatitis after eating food contaminated by an infected food-handler, 96 were investigated. In most of these, hepatic functional tests gave abnormal results and biopsy of the liver of 68 showed histologic evidence of hepatitis in 51. Only three were icteric⁸⁴. Three cases of inapparent hepatitis discovered by laboratory tests during a routine study of Koreans also portrayed symptomless infection⁸⁵. By using sensitive procedures for detecting hepatitis, infection by transfusion occurred oftener than believed. Among 56 patients who had received blood, 10 had evidence of inapparent infection, but none was icteric. In two, evidence of hepatitis appeared within six weeks, and in two others hepatic disturbance persisted 10 months. The rate of inapparent to overt infection was estimated as 1:100⁸⁶. The three articles just referred to have examples of transient inapparent infections that account for undetected carriers who serve as sources of infection. The number of cases of hepatitis in the United States reached a peak in 1960-61 but has declined. The next 7-year cyclic peak may occur in 1968.

Viral hepatitis affects other tissues besides the liver. Inflammation and granulomas were detected in specimens of gastric and intestinal mucosa and of the kidneys. Mild anemia and hemolytic anemia occasionally were observed⁸⁷.

Since 1961, 87 cases of hepatitis occurred in persons in close contact with chimpanzees or other primates⁸⁸. The mode of infection suggested airborne transmission which seemed possible, but thus far is unproved.

There are three or more serotypes of the

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causal hemovirus. Inoculation with tissue-cell cultures caused hepatitis in four of 15 volunteers. Hepatitis has a spectrum of severity ranging from inapparent infection to fatal jaundice. Hemoviruses are prevalent in healthy persons without their having had known hepatitis⁸⁹. If epidemic hepatitis and serum hepatitis are caused by the same viruses, but differ clinically according to the portal of entry, one wonders why gammaglobulin protects against one and not the other.

Strain WW-55 virus caused mild hepatitis in inoculated West African monkeys, the first time that this has been accomplished⁹⁰. Treatment of plasma with propiolactone and ultraviolet radiation was said to eliminate the danger of transmission of the virus⁹¹. Several authorities do not believe that the viruses of hepatitis have been isolated.

As in the case of viral hepatitis just mentioned, there has been a tendency to regard many viruses as specifically unitropic, but evidence accrues that other tissues also are affected. The myocardium, the gastrointestinal and neural system may be invaded by enterorepiratory and varicella viruses; herpes zoster may be disseminated especially in victims of lymphoma and in those treated with corticosteroids⁹²; and various tissues are involved in mice inoculated with the virus of lymphocytic choriomeningitis⁹³. Disturbed renal function and viruria occurred in victims of mumps. The virus may cause renal lesions⁹⁴ and induce occasional transitory nephritis. To see if the kidneys were the site of viral multiplication, and to account for viruria, attempts were made to recover viruses from the kidneys of children at necropsy. From 158 specimens, 84 yielded viruses, but the number decreased with increasing age of the subject. Cytomegalo-, adeno-, measles, varicella and Coxsackie viruses were recovered. In five instances, the isolated virus probably was related to the disease of the child. The others probably were commensals⁹⁵.

Recently, when antismallpox vaccination was widespread in England and Wales, 185 persons had eczema vaccinatum. More than half of them were accidentally inoculated and 6% died. Vaccination may be hazardous in hypersensitive people⁹⁶. Acute genual arthritis occurred 12 days after vaccination against smallpox. The virus of vaccinia was present in the synovial fluid⁹⁷. Doubt has been cast on the need for routine general vaccination in the United States.

Enteroviral Infection. Apprehension was raised by the occurrence of 87 reported cases of poliomyelitis-like illness associated with or

caused by orally administered antipolio vaccines. It was not possible always to determine if vaccines caused infection. Fifty-seven suspected cases, mostly in adults, occurred 4 to 28 days after vaccination. For that reason a suggestion was made, but with dissent, not to vaccinate persons more than 18 years of age, except under circumstances of unusual risk. The danger of vaccine causing serious infection is minimal, considering the millions of persons so treated⁹⁸. Concurrent enteroviral infections interfere with the action of polio vaccine⁹⁹.

In a study of the cause of sudden unexpected death of infants, ECHO viruses Types 7 and 22 were isolated from 7 of 10 babies¹⁰⁰. Whether or not the viruses were pathogenic was uncertain. Enteroviruses were "typed" successfully by complement-fixation. The technic was reliable and correlated with neutralization tests¹⁰¹. The clinical aspects of enteroviral infections in general were reviewed by Altman¹⁰².

Viral Dysentery. Bacteria were the chief causes of diarrhea among 214 Puerto Rican children. Coxsackie and ECHO viruses were isolated from 22% and specific immune bodies appeared in the blood of most. Mixed viral, bacterial and parasitic flora were present in 23%¹⁰³.

"Epidemic collapse" affected 404 pupils in three schools in Coventry in 1964. The features were frontal headache, nausea, vertigo, collapse abdominalgia, sore throat, cough and vomiting. Diarrhea occurred in only 11%. A virus was suspected as the cause¹⁰⁴. This infection also is called epidemic nausea and vomiting and seems to be similar to epidemic viral dysentery except for the infrequency of diarrhea¹⁰⁵.

Meningoencephalitis. St. Louis encephalitis virus exists in human serum, in domestic pigeons, mice and in mosquitoes of South and Central America, the West Indies and Florida as reported on in seven papers in the May, 1964, issue of the American Journal of Tropical Medicine. An epidemic of St. Louis encephalitis occurred for the first time in Pennsylvania and New Jersey. Sixty-four cases and five deaths were reported, but many more mild cases, no doubt, were undiagnosed and uncounted.

Reoviruses were recovered from the stools of three children with encephalitis and hepatitis. The viruses could not be proved to be the cause except for the presence of virus Type 1 in the stools and in the brain in one fatal case with myocarditis and interstitial pneumonia¹⁰⁶. Herpes simplex virus was recovered from the brain of a child with encephalitis¹⁰⁷.

Two adults had three or four attacks, and two children had two attacks of meningoencephalitis at intervals of four months to eight years. Coxsackie B5 and B2, and ECHO 1 and 7 apparently were the causes. The same virus or different ones may cause successive infections¹⁰⁸.

Road building in Liberia favored the spread of the tsetse fly from endemic areas of Gambian encephalitis. The flies now are a dangerous roadside hazard¹⁰⁹.

Eight of 520 bats in New England had evidence of infection with rabies virus, but only 3 seemed sick at the time of study. The authors were apprehensive of the spread of infection to other forms of wild-life¹¹⁰. It is more likely, however, that rabies was always endemic in the region and is not apt to "spread" anew. Rodents rarely transmit rabies to man. Among 50,000 rabid animals only 199 (0.42%) were rodents; 82 were squirrels¹¹¹. Attempts are underway to collect serum from vaccinated veterinarians as a substitute for hyperimmune horse serum that causes serious reactions. Apparently many persons receive antirabic vaccine unnecessarily. An estimated 30,000 people were so treated annually. In August a bite by a skunk caused the first reported case in the United States in 1964. Immediate vaccination failed to prevent death. In Brazil improperly prepared vaccine caused fatal post-vaccinal encephalomyelitis in 18 of 66 persons¹¹². One wonders if more persons die from vaccination than from rabies. Inapparent attacks and mild rabies never have been observed in man. Nevertheless, according to Bell's experiments, recovery is possible since 33% of his mice survived after inoculation¹¹³.

Russian scientists believe that a variant of rabies virus may cause multiple sclerosis and acute disseminated encephalomyelitis. Another virus suspected to cause amyotrophic lateral sclerosis is being investigated in the U.S.A.¹¹⁴.

Hemorrhagic Fevers. The hemorrhagic fevers of Asia seem to be caused by one or more viruses possibly related to dengue virus¹¹⁵. Dengue viruses were isolated from victims of hemorrhagic fever in Singapore, where the disease generally was mild except in young children¹¹⁶. A similar disease called Machupo observed in South America was caused by a virus similar to Junin virus and probably is transmitted by a wild rodent¹¹⁷. One wonders if this is a "new" disease or one that has come to attention. Hammon warned that *A. aegypti* mosquitoes may spread infection to the southern United States and elsewhere. To

account for the disease, he suggests that a dengue virus acquired unusual pathogenicity by genetic transformation¹¹⁸. If the Junin or Machupo viruses are similar to the Asian viruses, and if all are members of the dengue group, it is likely that they are antigenically related, but not necessarily mutant forms.

An accidental infection in a laboratory worker with the virus of louping-ill had features similar to Kyasanur Forest disease and Omak hemorrhagic fever¹¹⁹. Thrombocytopenia and bleeding are common to each, but also to dengue and other viral diseases.

In a flurry of papers, thrombocytopenia and purpura were described as peculiar to dengue¹²⁰, mumps¹²¹, rubella¹²², and infectious mononucleosis¹²³. A diminution of circulating platelets during pneumococcal pneumonia and compensatory thrombocytosis shortly after were described 40 years ago¹²⁴, and during typhus in 1929¹²⁵. Similar changes induced in inoculated animals resulted in purpura. Thrombocytopenia apparently is a common occurrence during infectious diseases.

Newly Recognized and Unusual Viral Diseases. Knowledge of epidemic neuromyasthenia of unknown cause was reviewed¹²⁶. A "new" or hitherto undescribed dermatosis was characterized by fever, leukocytosis and painful dermal plaques with dense infiltrations of neutrophil cells. Tetracycline had no therapeutic effect but cortisone caused rapid improvement¹²⁷. A peculiar epidemic infection with a papulo-vesicular rash on the hands and feet, called "Summer-term blains" affected 90 of 488 school-girls in England. A virus was suspected as the cause but none was isolated¹²⁸. Chagres virus was isolated from persons in Panama^{128a}. A man exposed to epizootic bovine abortion died from pneumonia caused by an agent of the bedsonia group similar to the cause of the bovine disease¹²⁹.

Mink disease of probable viral or mycoplasmal origin caused hypergammaglobulemia like that of multiple myeloma. A virus of mouse lymphosarcoma caused hypergammaglobulemia, plasma cell infiltration and amyloidosis. Amyloid nephrosis occurred in the late stage of lymphocytic choriomeningitis¹³⁰.

A virus that seemed to be the cause of human warts was cultivated *in vitro*¹³¹. The virus of Venezuelan equine encephalomyelitis was isolated from the marrow late in the disease when it was not found elsewhere in the body. The procedure may be applied successfully for the diagnosis of other viral infections¹³².

Miscellaneous Viral Studies. "Hospital

infections" caused by staphylococci and salmonellas are of serious import, but other microbes also are blamed. Chief among these are the viruses of hepatitis, smallpox, poliomyelitis, Coxsackie and ECHO disease, herpes simplex, vaccinia and respiratory tract infections¹³³. Viruses may be transmitted by contaminated enema tubing¹³⁴. Although viruses were present only in the central neural system in seven of 48 dead infants, they have not been proved to be the causes of unexplained sudden deaths¹³⁵ as mentioned previously.

More knowledge of "slow acting" viral infections of animals may shed light on the cause of some obscure human maladies. Ovine diseases such as scrapie, maedi and visna, and perhaps mink disease, are examples. They have characteristics resembling lupus erythematosus, rheumatoid arthritis, myeloma, polyarteritis, multiple sclerosis, pneumonia and encephalitis¹³⁶.

An interferon-like substance produced by herpes simplex virus suppressed the activities of vaccinia, herpes and influenza viruses. Because antibody to herpes simplex seems to have no effect on the infection or in preventing it, interferon may regulate the host-virus equilibrium¹³⁷. Interferon in the crusts of vaccinia lesions may be a nonfunctional response to viral growth or may suppress viral growth until an immune mechanism evolves. It also may modify the clinical course of smallpox¹³⁸.

Antiviral Agents. The antiviral activity of IDU (5-iodo-2' deoxyuridine) may depend upon the short intermolecular distance between the iodine and oxygen of a carbonyl group¹³⁹. The agent not only inhibited the multiplication of Rous sarcoma virus *in vitro*, but suppressed the transformation of cells into malignant ones¹⁴⁰. A combination of 5-bromo-deoxyuridine and N-methyl-isatinthiosemicarbazone eradicated vaccinia virus from cultured cells¹⁴¹.

Views on the efficacy of IDU to cure vaccinia and herpetic keratitis and dermal herpes are at variance¹⁴². In experimental studies, infected rabbits that were treated improved temporarily, but infection persisted. Similar disappointing results ensued in patients¹⁴³. In one study, treatment with IDU delayed healing. Another drug, tri-fluorothymidine may be of value in therapy¹⁴⁴. IDU failed in the treatment of herpes zoster¹⁴⁵, cutaneous herpes simplex¹⁴⁶ and trachoma¹⁴⁷ and 5-fluorodeoxyuridine had no effect on rubella virus in cell-cultures¹⁴⁸.

Amantidine inhibited the growth of influenza virus *in vitro*. Therapeutically, the agent had

antiviral activity in mice inoculated with the virus if given within 72 hours of infection¹⁴⁹. It also inhibited the growth of rubella virus¹⁵⁰. Viractin (actidione) from *Streptomyces griseus* had doubtful value for respiratory tract infections¹⁵¹. Sulfamethoxypyridazine was said to cure trachoma¹⁵², and a vaccine seemed to be effective for prevention¹⁵³. Other antiviral agents under study are: halogenated pyrimidine nucleosides for herpes viruses, hydroxybenzylbenzimidazole and guanidine for picorna viruses, and pteridines and cyclopin for others.

Improvements in the diagnosis and treatment of cutaneous viral infections were reviewed¹⁵⁴.

A thiosemicarbazone (methisazone) said to be of value as a prophylactic agent against smallpox in India, gave disappointing results in South Africa¹⁵⁵. It has no therapeutic value.

Viruses and Neoplasia. Because of evidence relating viruses to the cause of leukemia, the Congress of the United States authorized ten million dollars to support further research for these reasons: Virus-like particles were found in 30% of children with acute leukemia; the particles were structurally the same in human and animal leukemias; virus-like particles were transmitted in mouse milk to infant mice; and a hope that vaccines to prevent leukemia may be developed¹⁵⁶.

Electronmicroscopy disclosed discrete virus-like particles in human embryonic tissue infected with material from the bone marrow of patients with leukemia¹⁵⁷, but similar particles occasionally were seen in control cultures¹⁵⁸. Microbes isolated from leukemic children either were viruses or mycoplasmas that caused leukemia-like disease in inoculated mice. They were not found in normal or leukemic adults. Confusingly, similar microbes were isolated from children with sarcomas and with lupus erythematosus¹⁵⁹. The usual question of the presence of commensals activated by impaired host-resistance pertains. Viral and mycoplasmal particles obtained from human leukemic tissue appeared in the viscera of marmosets inoculated therewith. A relation between the particles and leukemia was not established, but similar ones have been found in leukemic mice, not in normal ones according to Domchowski's report at a recent meeting. On the other hand, neither Girardi nor Phillips and their co-workers were able to isolate viral agents from children with acute leukemia or with infectious mononucleosis^{160, 161}. Epidemiologic research so far has not revealed convincing evidence of a virus-like spread of leukemia in man^{162, 163}.

In an attempt to "interfere" with the

presumed virus of leukemia, a variety of viral vaccines was injected into a patient with acute leukemia. Periods of temporary clinical improvement occurred¹⁶⁴. Injection of gamma-globulin with antimicrobics had no beneficial effect on febrile infections during acute leukemia¹⁶⁵.

A Reo virus was isolated from a patient with Burkitt's lymphoma that seems to be endemic in Africa¹⁶⁶. Virus-like inclusions were present in marrow cells of three patients with multiple myeloma, but not in 15 other victims¹⁶⁷.

The prospects for establishing a causal role of viruses in human malignancy were outlined by Hilleman¹⁶⁸, Andrewes¹⁶⁹ and Enders¹⁵⁷ suspected that some cancers in man either may be caused by viruses or that viruses like other irritants serve as incitants.

Inoculated SV40 virus disappeared rapidly from infant hamsters but reappeared in tumors. Virus was not always present and seemed not to be essential to the retention of oncogenicity. Neutralizing antibody appeared in some animals, but was unrelated to the subsequent appearance of tumors¹⁷⁰. Cells infected with SV40 virus synthesized viral antigen and also the specific antigen of induced tumors. DNA inhibits the formation of the viral antigen and serves to differentiate the two¹⁷¹. An X-irradiated SV40 transplant as a vaccine prevented tumor formation in newborn hamsters inoculated with SV40 virus¹⁷². Tumor cells produced by SV40 virus in hamsters did not yield the virus on culture, but when seeded onto sensitive indicator cells, characteristic viral lesions appeared. The tumor cells evidently harbored persistent viral subinfection called the "virogenic state." Tumor cells induced by adenovirus Type 12 and polyoma virus failed to show viral subinfection. Evidently, basic differences occur in cells transformed by different viruses¹⁷³.

Adenoviral particles recovered from tumors induced by virus Type 12 were similar to the inoculated ones, but were "incomplete" suggesting why the living, infectious virus could not be isolated despite serologic evidence of its activity¹⁷⁴. Among a variety of viruses including adenoviruses, influenza, RS, mumps, measles, rhino-, polio, varicella and others, only adenoviruses 12, 18 and especially Type 7 caused tumors in inoculated newborn hamsters¹⁷⁵. Tumors appeared after long latent periods and were free of detectable viruses¹⁷⁰. Adenovirus Type 12 transformed hamster cells *in vitro* to morphologically altered cells, but whether the changed cells were malignant was

not determined¹⁷⁶. The oncogenicity of adenovirus Type 12 in hamsters was inhibited or prevented by the later administration of large amounts of the virus. The larger the quantity of virus inoculated initially, the fewer tumor-free animals¹⁷⁷.

Because adenovirus 12 induces sarcomas in newborn hamsters, persons who have been infected with the virus should be observed for years. Antibody studies indicated that about 25% of children and 48% of adults have had such infection, often inapparently. In one laboratory, Type 12 virus comprised only 3% of all adenoviruses isolated from 7,000 patients in four years¹⁷⁸.

According to several investigators, "there is no definitive information at present to relate any known virus to neoplasia in man"¹⁷⁵. Perhaps only a genetic portion of a virus¹⁷⁹ is responsible or a virus may act as an accelerator to chemical or hormonal induced neoplasias which would develop anyway¹⁸⁰. The problem is summarized in Chapters 15 to 19 of a recently published book¹⁸¹.

Bacillary Infections

Tuberculosis. Although a number of sanatoriums for tuberculosis have been closed or used for other purposes, the incidence of tuberculosis has risen in the United States in recent years¹⁸². Some authorities feel that since anti-polio vaccine has been so successful, had BCG vaccination been widely practiced, a similar decline in tuberculosis might have ensued. Other observers recommend BCG vaccination only for special groups likely to be infected. Its value in protecting against late postprimary tuberculosis is doubtful. Vaccination destroys the value of the tuberculin test to locate sources of infection and for diagnosis¹⁸³. According to Dubos, BCG vaccine evokes strong and lasting immunity only if the nature and quantity of a standard strain of bacilli used are correct, and if the vaccinees are able to produce antibody. At best, acquired immunity does not prevent the primary establishment of lesions nor does it result in the immediate eradication of super-infecting bacilli. Unfortunately, vaccination may prove to have limited usefulness even in unhygienic social environments¹⁸⁴. Thus the controversy continues.

The hope for the eradication of tuberculosis is dim for several reasons: (a) failure to detect and report cases, (2) failure of victims to accept therapeutic management, and (3) failure to prevent inactive disease from reactivating¹⁸⁵.

Deaths from tuberculous meningitis have de-

clined after modern therapy, but serious sequels are common among survivors. Among 65 of them, intracranial calcifications ensued in 21, auditory disturbance in 26, and abnormal electroencephalograms in 47. Normal education was possible in only 35¹⁸⁶.

Continued surveillance of previously untreated patients has not disclosed an increasing resistance of *Myco. tuberculosis* to antimicrobics. Less than 2% of strains resisted streptomycin and isoniazid and 2.2% resisted paraaminosalicylic acid¹⁸⁷.

"Atypical" Tubercle Bacilli. These bacilli cause pulmonary disease, lymphadenopathy, generalized infection, and destructive polyarthritis¹⁸⁸ indistinguishable from classic tuberculosis. Skin testing with various tuberculin also suggests the existence of inapparent infections. Both crossreactions to various antigens and multiple infections probably occur¹⁸⁹. The skin reactivity of 947 white infants and children indicated a higher incidence of infection with nonchromogenic atypical tubercle bacilli than with *M. tuberculosis* and skotochromogens. Among coloured patients, the relative incidence was reversed¹⁹⁰.

Uncertainty persists in regard to the origin of mycobacteria that are regarded as atypical, anonymous or unclassified. Some authorities believe them to be separate, distinct strains; and others, that they are variant forms of *M. tuberculosis*. Perhaps both views are valid. In my own experiments, culture of a strain of standard H37Rv for months or years on solid or in liquid media evoked several variant forms that had many, most, or all of the features of "atypical" strains¹⁹¹.

Leprosy. Immigrants from Indonesia increased the number of lepers in Holland to 250. Within months after arrival, supposedly cured patients had exacerbations¹⁹². Two patients who failed to improve after therapy with a sulfone compound (Dapone) were infected with bacilli resistant to the drug¹⁹³. Capreomycin was used successfully to control infection with *Myco. leprae* in the foot-pads of mice. It may have value in treating human victims¹⁹⁴.

Tetanus. In a 10-year period, 2,130 cases of tetanus were admitted to hospitals in Bombay. Eleven patients (0.5%) had had tetanus before; one of them three times. The intervals between attacks varied from three months to five years. All except one recovered. Six of the eleven were hypersensitive to antitetanus serum given for the initial attack. Recurrences may be due to the persistence and reactivation

of the original infection or to a new exogenous infection, indicating the need for active immunization in such persons. Apparently little or no active immunity ensues as the result of an attack of tetanus¹⁹⁵ in some cases.

Active immunization against tetanus with toxoid is the method of choice. Unimmunized persons who need protection should be given human tetanus immune globulin for quick action. Tetanus antitoxin is not reliable and there is danger of reaction to equine or bovine serums¹⁹⁶. The use of homologous antitetanus serum that has half-life 10 times longer than serum from other species would eliminate the danger¹⁹⁷. Penicillin protected mice against tetanus only when given within four hours after infection, but spores persisted unharmed¹⁹⁸.

Nine patients with tetanus were said to be cured promptly by hyperbaric oxygenation therapy⁹⁹. If *Cl. tetani* were active and were suppressed by oxygen, such treatment conceivably may be effective. But the toxin presumably is bound to neural tissue and the symptoms appear long after bacilli have ceased to grow or have disappeared. If oxygen therapy is curative, its mode of action is obscure.

While tracheostomy occasionally is life-saving when less traumatic measures fail, serious sequels may follow. Among 29 patients so treated, 23 lived more than three days and of these, 18 wounds became infected, eleven by staphylococci and five by *Pseudomonas*²⁰⁰. In another report, complications followed tracheotomy in 33% of 212 patients, 6 of whom died²⁰¹. Tracheostomy is greatly overdone.

Parenteral injection of medicaments caused infection with *Cl. welchii* in five patients, three of whom died²⁰². When the buttocks are the site of injection, it is surprising that such incidents are so rare. For this infection, hyperbaric oxygen therapy has a logical base for use against actively growing anaerobes. Some non-cytopathogenic viruses caused cytopathic effects in tissue cultures when subjected to 95% oxygen under pressure, but not in air²⁰³.

Salmonella. An epidemic of 23 cases of infection with *Salmonella infantis* probably came from eggs contaminated by a carrier. The disease generally was mild, and in one patient it was clinically inapparent. Despite the indication that the bacilli were sensitive by the tube-dilution test, both tetracycline and chloramphenicol failed in treatment²⁰⁴. No one knows why all salmonellas except *S. typhosa* resist chloramphenicol.

In a 3-month period, 745 cases of *S. newport* infection occurred. These were acquired from

bakery products in Upsala. About 66 per cent of victims were inapparently infected; the rest were sick in varying degrees of severity; and one died²⁰⁵. *Sal. typhosa* phage Type A infected 26 persons in Harlow, England. The source probably was contaminated corned beef. One patient had fever but no symptoms, and a child had neither fever nor symptoms yet typhoid bacilli were present in the blood of both²⁰⁶.

Salmonella paratyphi B caused an epidemic in Scotland, affecting 188 persons in May, 1964. The source probably was a confection prepared with artificial cream, imported eggs or canned meat. Forty patients were symptomless with inapparent infection. Four victims who had other chronic disease died²⁰⁷.

Ampicillin (Penbritin) was said to have controlled typhoid in seven of eight patients²⁰⁸ and was credited in ridding the bacilli from seven of eight carriers²⁰⁹.

Hodgkins disease renders patients particularly susceptible to infection with *M. tuberculosis* and *Salmonella*. Three patients infected with *Salmonella* were observed, two of whom died²¹⁰. *Salmonella* also may invade victims of hepatitis and others whose resistance is impaired. Pet chicks, dogs and turtles are sources of infection²¹¹.

Shigella. A cell-free vaccine will be ready soon for clinical trial²¹². One wonders if its immunizing effect will be as poor as that from cholera and typhoid vaccines.

Esch. coli. During an epidemic of enteritis among infants, *E. coli* was present in the oropharynx of many symptomless carriers. The carrier rate was 33 per cent in households of neighbouring families and 0 per cent in more remote places. Airborne transmission seemed likely to have occurred²¹³. The percentage of strains of *Escherichia coli* resistant to neomycin increased from none in 1957-58 to 80 per cent in 1961-62²¹⁴.

Pseudomonas, unlike pathogenic staphylococci and salmonellas, seldom caused widespread "hospital" epidemics²¹⁵. Yet, during a 42-month period, 73 premature, congenitally defective, leukemic and otherwise debilitated children were infected with *Pseudomonas* in Wales. Hygienic surroundings, the use of sterile instruments and parenteral medicaments or fluids are the best measures for prevention. Polymyxin was used therapeutically but without decisive effect²¹⁶.

Among 100 patients with bacteremia caused by gram negative bacilli, the urinary tract was the source of infection in 65 per cent, the skin in 14 per cent. Fifty-five died. The commonest

pathogens were *Esch. coli* and *Klebsiella*. Such serologic diversity that specific identification was impossible. Thirty-five of 45 patients who had vasomotor failure died²¹⁷.

An unexpected observation concerned a factor in the serum of some patients with chronic bacterial infection that specifically favors an increased growth rate of the pathogen. Serum from a patient infected with *Pseudomonas* allowed their rapid growth, but inhibited the growth of *Esch. coli*. and *Proteus*²¹⁸.

Anthrax. Anthrax as an occupational disease affected 57 patients in a 10-year period in Massachusetts, and undiagnosed infections no doubt occurred. Infection does not confer immunity yet prophylactic vaccination was recommended. Antimicrobics were said to have been effective in therapy²¹⁹. Anthrax was fatal in a pipe-fitter who handled goat-hair insulation felt. Diagnosis was made when bacteremia was discovered postmortem²²⁰. Several persons were infected during an epidemic among bison in Canada²²¹. Anthrax still is prevalent in southwestern Iran where 25 victims were observed in a hospital and of these four died. Many more cases no doubt occur for which medical aid is not sought or is not available²²².

Cholera. Extensive physiologic studies, previously lacking, were made. Dehydration caused by a depletion of extracellular fluid. There is a normal, or greater than normal, flow of protein-free plasma through the normal appearing enteric membrane that is not resorbed. One patient required the intravenous injection of more than 60 liters (15 gallons) of fluid in five days. Experiments also showed that water and electrolytes can be restored orally when possible²²³. The suggestion that the loss of fluid was the result of disturbed permeability not caused by local inflammation of the enteric mucosa, the use of the copper sulfate dilution method to measure plasma viscosity, the design of the "cholera cot", trial of streptomycin, and a low death-rate of 5% mentioned in the paper had all been described 20 years ago after the 1945 epidemic of cholera in Chungking in a report²²⁴ to which no reference was made.

Unusual manifestations of brucellosis may cause diagnostic perplexity. Debono observed 18 patients whose symptoms and signs were mistaken for poliomyelitis²²⁵. Chronic suppurative of the liver or spleen occurs²²⁶.

Plague occurred as usual in India²²⁷. An American soldier contracted bubonic meningitis in plague in Viet-nam. Lymphogranulomatosis first was suspected. Diagnosis was made after

P. pestis was recovered from a guinea pig inoculated with spinal fluid²²⁸.

The cause of "endotoxin shock" still is vague. Shock cannot be prevented by antimicrobial prophylaxis and its treatment is unsatisfactory. It is probable in some instances that antimicrobics, if given, may liberate endotoxin by destroying enteric bacteria²²⁹. Early diagnosis and therapy was said to have reduced the death-rate from 70 per cent to 30 per cent in a hospital²³⁰.

Although the fluorescent antibody technique does not replace cultural and other diagnostic procedures, it was successful for making rapid diagnosis in epidemics of pertussis and of *Ech. coli* infections in a remote area²³¹.

Coccal Infections

Streptococci. Monthly injections of repository penicillin to serve as both prophylaxis and therapeutics were superior to intermittent injections in reducing the attack rates of streptococcal infections and rheumatic recurrences²³². Penicillin G or phenethicillin given orally are the drugs of choice for the treatment of acute hemolytic streptococcal infection in children. Recurrences happen, but some of them may be from exogenous reinfection, not from failure of therapy. Recovery occurred promptly in most patients so treated, and in 80 per cent of those given tetracycline. Treatment with tetracyclines did not result in quick cure. Treatment had to be changed for victims of scarlet fever because streptococci were not eliminated²³³. The failure of penicillin to eradicate streptococci from the throat in some instances may owe to the presence there of penicillinase-producing staphylococci^{234, 235}.

The problem persists of differentiating viral pharyngitis, the commoner infection which needs no treatment, from hemolytic streptococcal sore throat which does. Methods of accurate diagnosis were outlined by Stollerman. The recommended treatment is 600,000 units or more of benzathine penicillin G. Penicillin may be given orally in doses of 200,000 to 250,000 units four times daily for ten days. Erythromycin is substituted for patients sensitive to penicillin²³⁶.

Three patients thought to have poststreptococcal glomerulonephritis instead had widespread inflammatory and necrotizing vascular lesions. Streptococci seemed also to cause polyvasculitis, but the drugs used for therapy may have been responsible²³⁷. A follow-up study was made 10 years after a unique epidemic caused by streptococci-induced poststrepto-

coccal glomerulitis in 62 persons. No evidence of chronic renal disease was detected in 58²³⁸. Previous studies had shown that permanent harm rarely ensued. Group B beta-hemolytic streptococci (*Str. agalactae*) were the commonest causes of neonatal sepsis, accounting for 25% of infections²³⁹.

L-form colonies of Group A streptococci can be identified with their parent cocci because both contain a specific M protein detectable by an immunofluorescent procedure²⁴⁰. L-form of *Streptococcus fecalis* caused fatal septicemia in two patients^{240a}.

Rheumatic Fever. Unless infection with Group A hemolytic streptococci is treated with penicillin within 24 hours of its onset, rheumatic fever can ensue. The fluorescent antibody technique serves to identify streptococcal infection in that early period and obviates treatment of other infections not influenced by antimicrobics. Unfortunately, streptococcal infections may be symptomless and undetected.²⁴¹ Previously, evidence accrued that too early treatment of streptococcosis impairs the development of immunity.

A review of 4,500 cases of rheumatic fever over a 40-year period disclosed that its incidence has decreased somewhat and the mortality rate has decreased to a greater extent.²⁴² A Russian investigator described the pattern of changes in lesions of the myocardium.²⁴³

In another co-operative study, a previous report of the beneficial effect of therapy with cortisone was not confirmed. Prednisone did not terminate the course of rheumatic activity any better than aspirin, but was helpful in controlling the exudative phase of severe acute myocarditis in critically sick patients. Prednisone therapy therefore is not needed for treating acute rheumatic polyarthritis with or without mild or questionable carditis.²⁴⁴

Staphylococci. Airborne transmission of staphylococci, though it occurs, is not a common mode of spread, nor does bedding appear to be a major source. Important means are the transfer of cocci from the nose to the hands of attendants and to the patient, and from infected patients to the hands of other hospital personnel to the next person and so on. Results of studies also minimize the importance of environmental reservoirs of Group A streptococci. Transfer was limited to intimate contact with carriers. Staphylococcal infections are more difficult to control with penicillin than those caused by streptococci. Tetracycline given to a carrier of staphylococci increased their number in his nose and in the

surrounding air, and their spread to other persons²⁴⁶.

During a year, 213 patients with staphylococcal sepsis were admitted to a 17-bed isolation unit. Only 14 died from that infection, but 14 other deaths were caused by superinvading gram negative bacilli. About half were infected with untypable staphylococci resistant to penicillin, tetracycline and chloramphenicol. The types of staphylococci present in the noses of patients were not the same as those of their infections. Nursing personnel did not become carriers of patients' strains, nor did the carrier-rate increase among them. The present mortality-rate (31%) is about the same as it was in the patients during 1945 (28%), before staphylococci became antimicrobial-resistant²⁴⁷.

In a survey, 14 per cent of patients were infected after admission to a hospital. *Staphylococcus aureus* was the chief cause in 34% of these and gram negative bacilli in 22 per cent. Twenty-six per cent of the patients were receiving antimicrobics at the time²⁴⁸. Twenty-one of 25 patients with fulminating staphylococcal infections recovered after treatment with a combination of a semisynthetic penicillin and Fucidin²⁴⁹.

Further evidence was added to show that deliberate nasal colonization of harmless staphylococci prevented the invasion of heterologous virulent ones²⁵⁰. A staphylytic substance was isolated from a species of *Pseudomonas*^{250a}.

With the addition of new phages to the standard ones, more of the currently untypable staphylococci can be classified. Type UC-18, for example, caused 10% of infections in a hospital and resisted penicillin, tetracycline and streptomycin. The strain was absent in persons not in hospitals²⁵¹.

Pneumococcal Pneumonia. Between 1952 and 1963, 2,000 cases of pneumococcal pneumonia and 529 instances of bacteremia were observed in a hospital, indicating the continued prevalence of that infection. *Pneumococcus* Types 1, 7, 8, 4, 3, 12, 14, 19, 6 and 2 in that order were the chief causes. Type 1 infection was associated with bacteremia in 66 per cent of cases. Type 3 gave the highest mortality, 51 per cent of 35 cases. The average death-rate without complications was 20 per cent; with complications, 53 per cent and with meningitis, 63 per cent. In adequately treated patients the death-rate in general was 12 per cent. Antimicrobial treatment was not always successful. It had little or no effect on the outcome among those destined at the onset of illness to die,

even when treatment began on the first or second days. These studies reemphasize the need to revive the procedure of type determination that is helpful in diagnosis, prognosis, therapy and epidemiology. The authors recommend specific vaccines for prophylaxis²⁵². Considering the relative rarity of lobar pneumococcal pneumonia, and the multitude of vaccines available against other infections, the procedure is impracticable excepting for small epidemics of pneumococcosis in closed populations.

Purulent meningitis in adults usually was caused by pneumococci or meningococci in a Detroit hospital between 1943 and 1963 and there has been no increase in the incidence of other gram positive or gram negative bacterial infections. Despite modern therapy, the mortality-rate of pneumococcal meningitis was 68 per cent²⁵³. The death-rate of *Klebsiella pneumoniae* meningitis was reduced from 98 per cent to 50 per cent. The infection occurred chiefly in debilitated patients among the 153 cases on record²⁵⁴.

For therapy, attempts often are made to secure large amounts of an antimicrobial in the spinal fluid²⁵⁵, as if the bacteria floating therein are harmful. Intravenous injection to achieve high concentration of the agent in the meningeal tissue at the site of infection is more logical.

Serious outbreaks of meningococcal meningitis afflicted recruits in military centres and elsewhere in the western United States. Apparently antimicrobial prophylaxis failed and other methods were applied to stop the disease. In one area, 15 of 105 victims died²⁵⁶. *Meningococcus* Type 2, Group B, became resistant to sulfonamides. A high carrier-rate persisted among persons treated orally with sulfadiazine or penicillin²⁵⁷.

Venereal Diseases

Modern aspects of syphilis and other treponemoses, gonorrhea, lymphogranuloma venereum, granuloma inguinale and nonvenereal genital diseases were discussed in several articles in the Medical Clinics of North America of June, 1964. A few points of interest are that about 65 per cent of untreated victims of syphilis have little inconvenience therefrom and that both syphilis and gonorrhea have increased in incidence. Indiscriminate penicillin therapy probably has inadvertently cured patients with either infection. At present, most syphilitic patients are treated by private physicians and perhaps 90 per cent of cases are not reported to health officers. The modern treatment of syphilis was outlined.

The standard serologic diagnostic tests for syphilis sometimes fail. In one study, negative reactions were obtained in 24 proved infections. The faulty result in 16 of them was caused by a positive prozone reaction²⁵⁸. Among 66,000 Austrian soldiers who donated blood to a blood bank, the VDRL test gave a positive reaction in 49. Thirty-nine of these had syphilis²⁵⁹. If the test is not wholly reliable, one wonders how many cases were missed or misdiagnosed.

Not long ago, suggestion was made that syphilis gradually evolved from the prototypes of yaws and bejel. A more recent view casts doubt on the separateness of the treponemes of venereal syphilis, endemic syphilis, bejel yaws and pinta. Perhaps the same microbe causes each disease and the different clinical responses may depend upon epidemiologic factors, the mode of transmission, the site of entry and the resistance of the human hosts. The incidence of atypical forms of infection may depend upon the frequency of febrile malaria in some areas of the world. Treponemes do not survive at temperatures higher than 40°C.

Improved methods of treatment have had no effect on the spread of gonococcal infection. Infections have increased in incidence worldwide and "the time has come for an entirely new attitude to this major source of human illness and unhappiness."²⁶⁰ After exposure to infected partners, 26 of 98 men had asymptomatic gonorrhea that was diagnosed by the fluorescent antibody procedure.²⁶¹ Falsely positive results may occur in tests of carriers of meningococci that share an antigen with the gonococcus.²⁶² Among 203 men with urethritis, *Gonococcus* was the cause in 139. The only microbe recovered from the rest was the T-strain of *Mycoplasma*. It resisted penicillin, but was sensitive to tetracycline. The infection probably represents the "sixth" venereal disease but may be asymptomatic at times.²⁶³ No viruses or evidence of their presence was discovered in 45 patients with nongonococcal urethritis.²⁶⁴ Immunofluorescent staining for the identification of *Tr. pallidum* and *N. gonorrhoeae* directly from smears of lesions can be done in about a minute²⁶⁵. The test also gave positive results in 7 of 42 patients with Reiter's syndrome and negative results in urethritis of other cause.²⁶⁶ Spectinomycin was said to be as effective as other antimicrobics for the treatment of acute gonorrheal urethritis.²⁶⁷

Mycotic Infections

Histoplasmosis. In 706 routine necropsy

studies, evidence of histoplasmosis previously undiagnosed or as an inapparent infection, was discovered in 85% of instances in the mid-western United States and in 12% elsewhere.²⁶⁸ A medical student contracted histoplasmosis in a laboratory. Studies then disclosed that 26 of 62 exposed classmates were sensitive to the histoplasmin, and nine had pulmonary infiltration.²⁶⁹ Direct staining of sputum is a reliable method of diagnosis.²⁷⁰ Soil polluted by bird droppings and sprayed with 36 gallons per 100 square feet of a 3% solution of formaldehyde was said to have reduced the incidence of histoplasmosis in an epidemic area.²⁷¹

According to Furcolow, attempts to control environmental exposure, sterilization of infected foci, and vaccines have not been successful in the eradication of histoplasmosis.²⁷² Amphotericin B is the drug of choice for the treatment of chronic histoplasmosis,²⁷³ but it must be used cautiously.

Histoplasmosis was discovered for the first time in Cyprus in two persons who were infected in a cave that harbored bats.²⁷⁴ In Colombia, *H. capsulatum* was present in a bat's liver.²⁷⁵ The disease had been known for years in Italy and the microbe was isolated from the soil near Bologna.²⁷⁶ Since 1963, 31 cases were recognised in Montreal.²⁷⁷ Many Puerto Ricans reacted positively to the histoplasmin skin test. In Japan, some agent other than *H. capsulatum* probably accounts for the rare reactors to the test.²⁷⁸ *H. duboisii* differs from *H. capsulatum*; in Africa lesions of the disease were in the skin, bone and abdominal viscera, not in the lungs or central nervous system. The epidemiology of the infection there is unknown.²⁷⁹

Coccidioidomycosis in the American Southwest was discussed by three essayists at the October 9 meeting of the American College of Physicians. The irregular distribution of the disease in endemic areas may be explained by differences in local soils and the temperature that either do or do not favor the existence of the fungus. The infection is clinically inapparent in 60 per cent of infected persons. Disease ranges in severity from mild respiratory tract discomfort to severe pneumonia and death. A chronic form occurs: Amphotericin-B is effective if therapy is prolonged, but as mentioned elsewhere in this review, it may be nephrotoxic.

The hazard of contracting coccidioidomycosis in the endemic area of the St. Joaquin Valley, 1963-64, was less than that reported previously. During the first year of residence,

infection was evident in only 1.58% of persons in the susceptible population. Suppression of dust was a factor in reducing the incidence²⁸⁰.

Among 1,895 persons who served in a laboratory where *Coccidioides immitis* was under study during 18 years, about 10 per cent gave evidence of having been accidentally infected. One third of those whose skin reacted to coccidioidin were asymptomatic. The rest had had dermal lesions or respiratory tract illness²⁸¹.

Among 22 patients with aspergillosis, 16 were leukemic and four had cancer. Of these, 20 had received corticosteroids, antimicrobics or antineoplastic drugs that impaired their resistance²⁸². Growth of *Candida albicans* was inhibited by the intact conjunctiva and extracts thereof. The inhibition was not ascribed to an antimetabolic action and was not caused by lysozyme²⁸³.

Cryptococcus neoformans usually is regarded as an opportunistic invader in patients whose resistance is impaired. A case was described, however, in a previously healthy youth who apparently contracted the infection from pigeon droppings. He had severe hepatitis, pneumonia, splenomegaly and lymphadenitis. In retrospect, a transitory attack of pleurisy and pulmonic invasion, suspected as tuberculous 19 months previously probably was cryptococcal in origin. Spontaneous remission then was followed by systemic dissemination. Subsequent therapy with amphotericin B was successful.²⁸⁴

Protozoal and Metazoal Infections

In 1936, 148 confirmed and presumptive cases of malaria were reported in the United States. *P. vivax* accounted for 78 cases and *P. falciparum* for 36. On a ship from Africa recently 40 persons had malaria. Twelve infections were caused by *P. falciparum* of which eight were overt and four were inapparent. Five other cases originated in the United States. Of these, two were caused iatrogenically, a third infection had been acquired years ago, and in two the origin was unknown.²⁸⁵ The fluorescent antibody test gave positive results in malarial infections.²⁸⁶

Diaprim (pyrimethamine) was used successfully in the prevention of infection in a hyper-epidemic region of Gambia. None of the protected children developed detectable antibody in contrast with untreated ones. Frequent reinfection also maintains specific antibody at a high level²⁸⁷. According to other investigators, Camolar (cycloguanil pamoate) also afforded long-term protection after a single intramuscular injection.²⁸⁸

Despite control programs, malaria is the most serious insect-borne disease in Central America. Mosquitoes have acquired resistance to synthetic antimalarial drugs. Malaria occurred among troops in Vietnam who received chloroquine and primaquine, and among Cambodians who were given amodiaquine. Evidently, the disappointing results are a serious setback in the control of the disease. Perhaps a return to the use of quinine is imminent.^{289, 290} There is evidence that *P. falciparum* may resist quinine.²⁹¹

It still is uncertain if different species of *Leishmania* account for the different clinical manifestations of infection as oriental sore (*L. tropica*), mucocutaneous disease (*L. braziliensis*) and kala azar (*L. donovani*) or if the microbe is the same in each and host resistance designs the form the disease takes. In the Sudan, six infected Americans were observed. Four of these had dermal ulcers only, and two had classic kala azar as if they were less resistant to the same microbe. Chloroquine had been used as an antimalarial agent in those who had dermal lesions, but not in those severely ill, as if the drug had a suppressive action on leishmania. Six persons who were not sick and without lesions reacted positively to the dermal leishmanin test, indicating that they, having a higher degree of resistance, had been inapparently infected.²⁹² Cutaneous leishmaniasis is widely distributed in forested regions of Central and South America. Treatment with pyrimethamine was said to be effective in therapy, but is toxic.

Chagas disease caused by *Trypanosoma cruzi*, endemic in Central and South America, is transmitted by several species of triatomine bugs. About 22% of Panamanians had serologic evidence of infection.

Schistosomiasis affects about 5 per cent of the world population. *S. japonica* causes the most serious infections. With increased travel in and from endemic regions, the infection is becoming more prevalent elsewhere.²⁹³

More than 600 cases of leptospirosis were recorded in the United States since 1953. Rats are not the only source of infection. Farmers, veterinarians, packing-house employees and meat inspectors are at risk. In the general population, 2.6 per cent of sera from persons gave positive results to serologic tests.²⁹⁴ *Ecchinococcus multicellularis* infected foxes and cows in midwest United States, Alaska and Canada.²⁹⁵

Trichinosis among 11 diners was treated with thiabendazole. The drug induced defervescence

of the disease and a sense of well-being in four victims. It failed to kill the larvae, caused dermatitis and central neural disturbance and did not alter the eosinophilia.²⁹⁶ The fluorescent antibody procedure was said to have greater diagnostic value than the precipitin test and the complement fixation test. It gave a positive reaction within two weeks of the onset of disease.²⁹⁷

Another antihelminthic drug, dithiazone iodide (Delvex) caused serious gastroenteric and other disturbances. Eight treated patients died. It should be used only for severe infection caused by *Trichiuris* or *Strongyloides*.²⁹⁸

Miscellaneous

Urinary Tract Infection.—Urinary tract and other infections caused by gram-positive bacteria have declined more than 50 per cent. in 12 years only to be replaced by infections with *Klebsiella*, *Aerobacter* and *Proteus*.²⁹⁹ The change in the flora probably was brought about by antimicrobial therapy. The problem of infection acquired in hospitals, particularly of the urinary tract was reviewed by Sanford.³⁰⁰

The lining of the urinary bladder is naturally able to destroy bacteria. Cystitis often heals and the urine becomes sterile.³⁰¹ The introduction of a retention catheter may not cause infection in a normal bladder.³⁰² Measurement of specific agglutinins in the blood was said to be helpful in the diagnosis of overt or inapparent pyelonephritis.³⁰³

Infections occurred in 26 of 30 patients in whom renal homotransplantation was done, and contributed to the cause of death in 10. *Staphylococci*, *Pseudomonas* and other gram-negative bacilli were the chief causes. Infections often followed immunosuppressive therapy that impaired the patients' defensive mechanism.³⁰⁴

Protoplasts, as bacteria without cell walls, persist in renal tissue after apparent cure of pyelonephritis and may account for a relapse of infection. Erythromycin killed protoplasts, but was ineffective against intact bacteria.³⁰⁵ Protoplasts and L forms were subjects of a symposium, the summary of which appeared in *Science* magazine of 5 February, 1965. Their possible causal relation to subacute bacterial endocarditis, rheumatic fever, Reiter's syndrome and other diseases was suggested.

Other Studies. The value of ultraviolet radiation in reducing the number of bacteria in surgical operating rooms was studied cooperatively in five hospitals. Differences in the number of surviving air-borne bacteria varied according to the nature of the infected

wounds. Irradiation reduced the risk of post-operative infection of clean wounds by 25 per cent. The net effect in all instances, however, was negligible, that is, infection occurred in 7.4 per cent of wounds in irradiated rooms and in 7.5 per cent of those in control areas. Infection rates varied from 3 to 11.7 per cent among the five institutions indicating that many other factors play a role in the incidence of post-operative infection.³⁰⁶

An account of contagious diseases among the English pilgrims on ship-board and after their arrival in America in the 1620's also describes the ravages of smallpox among the native Amerinds. They, not having been exposed to smallpox before, had no immunity. The decimation of hostile tribes was an important factor in the success of the immune or partially immune pilgrims in establishing permanent colonies.³⁰⁷ Similar circumstances, no doubt, pertained in Polynesia after measles was introduced by early explorers.

The thymus gland was said to play a key role in the maturation of immunologic capabilities by means of a humoral mechanism.³⁰⁸

Electronmicroscopy of microbes is advancing rapidly as shown by many articles in a symposium.³⁰⁹ An apparatus that magnifies billiomths of an inch is being constructed. My own studies visualized the penetration of bacilli into the enteric mucosa of rats. Apparently, these harmless commensals are disposed of by surface-action of the microvilli and superficial tissue, and by phagocytosis or bacteriocatalysis in enteric epithelial cells.³¹⁰

REFERENCES

1. WAKSMAN, S. A. (1965): Antibiotics: The Duplication Problem, *Science*, **147**, 1396.
- 1a. KLEIN, J. O., EICKHOFF, T. C., and FINLAND, M. (1964): Gentamycin: Activity in Vitro and Observations in 26 Patients, *Amer. J. med. Sci.*, **248**, 528.
2. KLEIN, J. O., *et al.* (1964): Cephalothin: Activity in Vitro, Observation and Excretion in Normal Subjects and Clinical Observations in 40 Patients, *ibid.*, **248**, 640.
3. BAINES, R. D., and RIFKIND, D. (1964): Intravenous Administration of Sodium Colistimethate, *J. Amer. med. Ass.*, **190**, 278.
4. PERKINS, R. L. (1964): Apnea with Intramuscular Colistin Therapy, *ibid.*, **190**, 421.
5. BARBER, M., and WATERWORTH, P. M. (1964): Penicillinase-Resistant Penicillins and Cephalosporins, *Brit. med. J.*, **ii**, 344.
6. GEDDES, A. M., SLEET, R. A., and MURDOCH, J. M. (1964): Lincomycin Hydrochloride. Clinical and Laboratory Studies, *ibid.*, **ii**, 670.
7. BARBER, M., and WATERWORTH, P. M. (1964): Antibacterial Activity of Lincomycin and Pristinamicin: A Comparison with Erythromycin, *ibid.*, **ii**, 603.

8. NOYES, R. W., *et al.* (1965): Drug Antagonism between Lincomycin and Erythromycin, *Science*, **147**, 746.
9. PINES, A., *et al.* (1964): Controlled Comparison of Lymecline with Tetracycline Hydrochloride in Exacerbations of Chronic Bronchitis, *Brit. med. J.*, **ii**, 1495.
10. BENNETT, J. E., *et al.* (1964): In vivo Activity of Colloidal Hamycin, an Antifungal Antibiotic, *Proc. Soc. exp. Biol. (N.Y.)*, **117**, 166.
11. KUCK, N. A., PEETS, E. A. and FORBES, M. (1963): Mode of Action of Ethambutol, on Mycobacterium, Strain H37Rv, *Amer. Rev. resp. Dis.*, **87**, 905.
12. Antimicrobial Agents and Chemotherapy, (1965): *Science*, **147**, 522.
13. WEINSTEIN, L., LERNER, P. L., and CHEW, W. A. (1964): Clinical and Bacteriological Studies of the Effect of Massive Doses of Penicillin G on Infections Caused by Gram-negative Bacilli, *New Engl. J. Med.*, **271**, 525.
14. GRAY, I. R., *et al.* (1964): Oral Treatment of Bacterial Endocarditis with Penicillins, *Lancet*, **ii**, 110.
15. KREIDBERG, M. B., and CHERNOFF, H. L. (1965): Ineffectiveness of Penicillin Prophylaxis in Cardiac Catheterization, *J. Pediat.*, **66**, 286.
16. WEINSTEIN, L., SAMET, C. A., and CHEW, W. H. (1964): Studies of the Effects of Penicillin-Sulfonamide Combinations in Man, *Amer. J. med. Sci.*, **248**, 408.
17. Many Drug-Resistant TB Cases Yield to New Therapy Approaches (1964): *Antib. News*, **1**, 1.
18. SCHOENWETTER, A. H., and SILBER, E. N. (1965): Penicillin Hypersensitivity, Acute Pericarditis, and Eosinophilia, *J. Amer. med. Ass.*, **191**, 672.
19. PAS, T. A., and QUINN, E. L. (1965): Cholestatic Hepatitis Following the Administration of Sodium Oxacillin, *J. Amer. med. Ass.*, **191**, 674.
20. VANARSDAL, P. P., and GILLILAND, B. C. (1965): Anemia Secondary to Penicillin Treatment, *J. Lab. clin. Med.*, **65**, 277.
21. ETTINGER, E., and KAYE, D. (1964): Systemic Manifestations After a Skin Test with Penicilloyl-polylysine, *New Engl. J. Med.*, **271**, 1605.
22. Chloramphenicol (1964): *Med. News, J. Amer. med. Ass.*, **190**, 34.
23. ROSENTHAL, R. L., and BLACKMAN, A. (1965): Bone-Marrow Hypoplasia Following Use of Chloramphenicol Eye Drops, *ibid.*, **191**, 136.
- 23a. Teratogenic Action of Actinomycin D. (1965): *Abstr. J. Amer. med. Ass.*, **191**, 136.
24. WAISBREN, B. A., and BROWN, I. (1964): Effect of Wide-Spectrum Antibiotics on Bactericidal Activity of Human Serum: In Vitro and in Vivo, *Amer. J. med. Sci.*, **248**, 56.
25. SHEAR, L., *et al.* (1965): Intraperitoneal Antibiotic Administration: Rate of Absorption Across Normal Peritoneum, *ibid.*, **249**, 1.
26. HARRIS, C. (1964): The Physician and Drug Disputes, *Science*, **146**, 717.
27. SMITH, T. J. (1964): Antibiotic-Induced Diseases, in *Diseases of Medical Progress*, Edit., R. H. Moser, pp. 3-60. Springfield, Illinois: Charles C. Thomas.
28. ANDREWES, C. H. (1964): The Complex Epidemiology of Respiratory Virus Infections, *Science*, **146**, 1274.
29. BUCKLAND, F. E., and TYRRELL, D. A. J. (1964): Experiments on the Spread of Colds, *J. Hyg. (Lond.)*, **62**, 365.
30. HAMPARIAN, V. V., LEAGUS, M. B., and HILLEMANN, M. R. (1964): Additional Rhinovirus Serotypes, *Proc. Soc. exp. Biol. (N.Y.)*, **116**, 976.
31. CATE, T. R., *et al.* (1965): Production of Tracheobronchitis in Volunteers with Rhinovirus in a small-Particle Aerosol, *Amer. J. Epidemiol.*, **1**, 95.
32. HAMPARIAN, V. V. *et al.* (1964): Epidemiologic Investigations of Rhinovirus Infections, *Proc. Soc. exp. Biol. (N.Y.)*, **117**, 469.
33. HILLEMANN, M. R. (1964): Prospects for Vaccination Against More Recently Discovered Respiratory Viruses, *Industry and Trop. Health*, **5**, 82.
34. HILLEMANN, M. R. (1964): A Forward Look at Viral Vaccines, with Special Reference to a New Immunologic Adjuvant, *Amer. Rev. resp. Dis.*, **90**, 683.
35. BLOOM, H. H., *et al.* (1964): Patterns of Adenovirus Infection in Marine Corps Personnel, *Amer. J. Hyg.*, **80**, 328.
36. SWANN, N. H. (1964): Acute Thyroiditis Associated with Adenovirus Infection, *Program Amer. Coll. Phys.*, Oct. 8, p. 30.
37. GRAYSTON, J. T., *et al.* (1964): Epidemic Keratoconjunctivitis on Taiwan: Etiological and Clinical Studies, *Amer. J. trop. Med. Hyg.*, **13**, 492.
38. BERCOVICH, S., and TARANKO, L. (1964): Acute Respiratory Illness in Premature Nursery Associated with Respiratory Syncytial Virus Infection, *Pediatrics*, **34**, 753.
39. GARDNER, P. S., ELDERKIN, F. M., and WAGNER, A. H. (1964): Serologic Study of Respiratory Syncytial Virus Infection in Infancy and Childhood, *Brit. med. J.*, **ii**, 1570.
40. HAMBLING, M. H. (1964): A Survey of Antibodies to Respiratory Syncytial Virus in the Population, *ibid.*, **i**, 1223.
41. BEEMS, M., EGERER, R., and ANDERSON, J. (1964): Respiratory Syncytial Virus Neutralizing Antibodies in Persons Residing in Chicago, *Pediatrics*, **34**, 761.
42. JOSKE, R. A., *et al.* (1964): Hepatitis-Encephalitis in Humans with Reovirus Infection, *Arch. intern. Med.*, **113**, 811.
43. KASEL, J. A., *et al.* (1965): ECHO Virus Type 25, Infection in Adult Volunteers, *Proc. Soc. exp. Biol. (N.Y.)*, **118**, 381.
44. BASHE, W. J., *et al.* (1964): Failure of Polyvalent Vaccine to Provide Clinical Protection against Asian Influenza, *New Engl. J. Med.*, **270**, 870.
45. HOBSON, D., *et al.* (1964): Serological Studies on Adult Volunteers Inoculated with Oil-Adjuvant Asian Influenza Vaccine, *Brit. med. J.*, **ii**, 271.
46. MOFFET, H. L., GRAMBLETT, H. G., and DOBBINS, J. (1964): Outbreak of Influenza A2 Among Immunized Children, *J. Amer. med. Ass.*, **190**, 806.
47. WOODS, C. A., and ELLISON, G. W. (1964): Encephalopathy Following Influenza Immunization, *J. Pediat.*, **65**, 745.
48. Flu Outbreaks Hit 21 States (1965): *AMA News*, Mar. 22, page 1.

48. NAYAK, D. P., *et al.* (1964): Progressive Descending Influenza Infection in Mice Determined by Immunofluorescence, *Proc. Soc. exp. Biol. (N.Y.)*, **116**, 200.
49. ATKINS, E., CRONIN, M., and ISACSON, P. (1964): Endogenous Pyrogen Release from Rabbit Blood Cells Incubated in vitro with Parainfluenza Virus, *Science*, **146**, 1469.
50. ARTENSTEIN, M. S., BELLANTI, J. A., and BUESCHER, E. L. (1964): Identification of the Antiviral Substances in Nasal Secretions, *Proc. Soc. exp. Biol. (N.Y.)*, **117**, 558.
51. KAPIKIAN, A. Z., *et al.* (1964): A Pilot Study of Acute Respiratory Illness on a College Campus, *Amer. Rev. resp. Dis.*, **90**, 175.
52. EVANS, A. S., and DICK, E. C. (1964): Acute Pharyngitis and Tonsillitis in University of Wisconsin Students, *J. Amer. med. Ass.*, **190**, 699.
53. PEK, S., and GIKAS, P. W. (1965): Pneumonia due to Herpes Zoster, *Ann. intern. Med.*, **62**, 350.
54. FORSYTH, B. R., *et al.* (1965): Etiology of Primary Atypical Pneumonia in a Military Population, *J. Amer. med. Ass.*, **191**, 364.
55. GRAYSTON, J. T., *et al.* (1965): Mycoplasma Pneumoniae Infections, Clinical and Epidemiologic Studies, *ibid*, **191**, 369.
56. REIMANN, H. A. (1964): Viral and Mycoplasma Pneumonias, *Dis. Chest*, **46**, 158.
57. SKOLDENBURG, B. (1965): Aseptic Meningitis and Meningo-Encephalitis in Cold-Agglutinin-Positive Infections, *Brit. med. J.*, **i**, 100.
58. REIMANN, H. A. (1944): Primary Atypical Pneumonia of Unknown Cause: Report of a Similar Disease without Pneumonia, *J. Mich. med. Soc.*, **43**, 147.
59. Infective Agent in Human Leukemia (1965): *Leading article, Brit. med. J.*, **i**, 267.
60. DOWDLE, W. R., and ROBINSON, R. Q. (1964): An Indirect Hemagglutination Test for Diagnosis of Mycoplasma Pneumoniae Infections, *Proc. Soc. exp. Biol. (N.Y.)*, **116**, 947.
61. LUDLAM, G. B., BRIDGES, J. B., and BENN, E. C. (1964): Association of Stevens-Johnson Syndrome with Antibody for Mycoplasma Pneumoniae, *Lancet*, **i**, 958.
62. Virus, Fungus, or Bacterium? (1964): *Science*, **146**, 1077.
63. CARMICHAEL, L. E., FABRICANT, J., and SQUIRE, R. A. (1964): A Fatal Systemic Disease of Infant Puppies Caused by Cytopathogenic Organisms with Characteristics of Mycoplasma, *Proc. Soc. exp. Biol. (N.Y.)*, **117**, 826.
64. GRIST, N. R., and McLEAN, C. (1964): Infections by Organisms of Psittacosis Lymphogranuloma Venereum Group in the West of Scotland, *Brit. med. J.*, **ii**, 21.
65. DEAN, D. J., *et al.* (1964): Prevention of Psittacosis, *Publ. Hlth. Rep. (Wash.)*, **79**, 101.
66. RIFKIND, D., *et al.* (1964): Transplantation Pneumonia, *J. Amer. med. Ass.*, **189**, 808.
67. HEDLEY-WHITE, E. T., and GRAIGHEAD, J. E. (1965): Generalized Cytomegalic Inclusion Disease after Renal Homotransplantation, *New Engl. J. Med.*, **272**, 473.
- 67a. HANSHAW, J. B., *et al.* (1965): Acquired Cytomegalovirus Infection, *New Engl. J. Med.*, **272**, 602.
68. PHILLIPS, C. A., *et al.* (1965): Isolation of Rubella Virus. An Epidemic Characterized by Rash and Arthritis, *J. Amer. med. Ass.*, **191**, 615.
69. RUDOLPH, A. J., *et al.* (1965): Transplacental Rubella Infection in Newly Born Infants, *ibid*, **191**, 843.
70. First Trimester Rubella Isolated after Delivery (1965): *Antibiot. News*, **2**, 3.
- 70a. HARDY, J., *et al.* (1965): Postnatal Transmission of Rubella Virus to Nurses, *J. Amer. med. Ass.*, **191**, 1034.
71. BRODY, J. A., SEVER, J. L., and SCHIFF, G. M. (1965): Prevention of Rubella by Gammaglobulin During an Epidemic in Barrow, Alaska, in 1964, *New Engl. J. Med.*, **272**, 127.
72. Gap in Rubella Defenses, *Mod. Med.*, May 25, 1964, p. 29.
73. SEVER, J. L., SCHIFF, G. M., and HUEBNER, R. J. (1964): Rubella Antibodies in Pregnant Women, *Obstet. Gynec.*, **23**, 153.
74. Salivary Gland Virus may Equal Rubella Fetal Peril (1964): *Antibiot. News*, **1**, 1.
75. BRODY, J. A., *et al.* (1964): Measles Vaccine Field Trials in Alaska, *J. Amer. med. Ass.*, **190**, 965.
76. New, Further Attenuated Live Measles Vaccine Tested in 6,000 Children (1964): *Med. News*, *ibid*, **190**, 27.
77. HOAGLAND, R. J. (1964): The Incubation Period of Infectious Mononucleosis, *Amer. J. publ. Hlth.*, **54**, 1699.
78. SMITH, D. R. (1964): Postperfusion Febrile Syndrome, *Brit. med. J.*, **i**, 945.
79. SELLING, B., and KILBRICK, S. (1964): An Outbreak of Herpes Simplex among Wrestlers (Herpes Gladiatorum), *New Engl. J. Med.*, **270**, 979.
80. WHEELER, C. E., and HUFFINES, W. D. (1965): Primary Disseminated Herpes Simplex of the Newborn, *J. Amer. med. Ass.*, **191**, 455.
81. NIGOGOSYAN, G., and MILLS, G. W. (1965): Herpes Simplex Cervicitis, *ibid*, **191**, 496.
82. CHEEVER, A. W., VALSAMIS, M. P., and RABSON, A. S. (1965): Necrotizing Toxoplasmic Encephalitis and Herpetic Pneumonia Complicating Treated Hodgkins Disease, *New Engl. J. Med.*, **272**, 26.
83. SHEARER, M. L., and FINCH, S. M. (1964): Psychosis with Recurrent Herpes, *ibid*, **1964**, 494.
84. SPONG, F. W., *et al.* (1964): Anicteric Hepatitis: A Population Study, Program, *Amer. Coll. Phys. Oct. 18*, p. 4.
85. CHUNG, W. W., *et al.* (1964): Anicteric Hepatitis in Korea. I. Clinical and Laboratory Studies, *Arch. intern. Med.*, **113**, 526.
86. HAMPERS, C. L., PRAGER, D., and SENIOR, J. R. (1964): Post-Transfusion Anicteric Hepatitis, *New Engl. J. Med.*, **271**, 747.
87. CONARD, M. E., SCHWARTZ, F. D., and YOUNG, A. A. (1964): Infectious Hepatitis—A Generalized Disease, *Amer. J. Med.*, **37**, 789.
89. McLEAN, I. W. (1964): Clinical Significance of Recent Investigation of Hepatitis Viruses, *Postgrad. Med.*, **35**, 481.
90. Hepatitis Apparently Produced in an Experimental Animal (1964): *Med. News, J. Amer. med. Ass.*, **189**, 33.
91. Hepatitis Risks in Blood Plasma Held Eliminated (1964): *Antibiot News*, **1**, 1.

92. MERSELIS, J. G., KAYE, D., and HOOK, E. W. (1964): Disseminated Herpes Zoster. A Report of 17 Cases, *Arch. intern. Med.*, **113**, 679.
93. WILSNACK, R. E., and ROWE, W. R. (1964): Immunofluorescent Studies of the Histopathogenesis of Lymphocytic Choriomeningitis Virus Infection, *J. exp. Med.*, **120**, 829.
94. UTZ, J. P., HOOK, V. N., and ALLING, D. W. (1964): Clinical and Laboratory Studies of Mumps. IV. Viruria and Abnormal Renal Function, *New Engl. J. Med.*, **270**, 1283.
95. BENYESH-MELNICK, M., ROSENBERG, H. S., and WATSON, B. (1964): Viruses in Cell Cultures of Kidneys of Children with Congenital Heart Malformation and other Diseases, *Proc. Soc. exp. Biol. (N.Y.)*, **117**, 452.
96. COPEMAN, P. W. M., and WALLACE, H. J. (1964): Eczema Vaccinatum, *Brit. med. J.*, **ii**, 906.
97. SILBY, H. M., et al. (1965): Acute Monarticular Arthritis after Vaccination, *Ann. intern. Med.*, **62**, 347.
98. PHS Recommendations on Oral Vaccine Use (1964): Washington News, *J. Amer. med. Ass.*, **190**, 15.
99. FELDMAN, R. A., HOLGUIN, A. H., and GELFAND, H. M. (1964): Interference in Poliovirus Vaccination, *Pediatrics*, **33**, 526.
100. MOORE, M. L., et al. (1964): Sudden Unexpected Death in Infancy. Isolations of ECHO Type 7 Virus, *Proc. Soc. exp. Biol. (N.Y.)*, **116**, 231.
101. GNESH, G. M., PLAGER, H., and DECHER, W. (1964): Enterovirus Typing by Complement Fixation, *ibid*, **115**, 898.
102. ALTMAN, R. (1964): Clinical Aspects of Enterovirus Infection, *Postgrad. Med.*, **35**, 451.
103. GUARDIOLA-ROTGER, A., et al. (1964): Studies on Diarrheal Diseases, *J. Pediat.*, **65**, 81.
104. POLLOCK, G. T., and CLAYTON, T. M. (1964): "Epidemic Collapse": A Mysterious Outbreak in Three Coventry Schools, *Brit. med. J.*, **ii**, 1625.
105. REIMANN, H. A. (1963): Viral Dysentery, *Amer. J. med. Sci.*, **246**, 404.
106. JOSKE, R. A., et al. (1964): Hepatitis-Encephalitis in Humans with Reovirus Infection, *Arch. intern. Med.*, **113**, 811.
107. KENT, T. H., and NICHOLSON, D. P. (1964): Herpes Simplex Encephalitis, *Amer. J. Dis. Child.*, **108**, 644.
108. KEMOLA, E., and LAPINLEIMU, K. (1964): Multiple Attacks of Aseptic Meningitis in the Same Individuals, *Brit. med. J.*, **i**, 1087.
109. ABEDI, Z. H., and MILLER, M. J. (1964): Roadside Tsetse Hazard in Liberia, *Amer. J. trop. Med. Hyg.*, **13**, 499.
110. GIRARD, K. F., et al. (1965): Rabies in Bats in Southern New England, *New Engl. J. Med.*, **272**, 75.
111. Rabies Surveillance Unit, C.D.C. Atlanta (1964): The Role of Rodents in the Epidemiology of Rabies Morbidity and Mortality, **13**, 398.
112. Post-Vaccinal Rabies in Brazil (1965): *Trop. Med. and Hygiene News*, **14**, 8.
113. Laboratory Animals Survive Inoculation with Rabies Virus (1964): *Med. World News*, Sept. 11, p. 9.
114. BRODY, J. A., et al. (1965): Soviet Search for Viruses that Cause Chronic Neurologic Diseases in the U.S.S.R., *Science*, **147**, 1184.
115. HAMMON, W. M., and SATHER, G. E. (1964): Virological Findings in the 1960 Hemorrhagic Fever Epidemic (Dengue) in Thailand, *Amer. J. trop. Med. Hyg.*, **13**, 629.
116. GOLDSMITH, R. S., et al. (1965): Haemorrhagic Fever in Singapore, A Changing Syndrome, *Lancet*, **i**, 334.
117. WIEBENGA, N. H., et al. (1964): Epidemic Hemorrhagic Fever in Bolivia. II. Demonstration of Complement-Fixing Antigen in Patient's Sera with Junin Virus Antigen, *Amer. J. trop. Med. Hyg.*, **13**, 626.
- JOHNSON, K. M., et al. (1965): Virus Isolation from Human Cases of Hemorrhagic Fever in Bolivia, *Proc. Soc. exp. Biol. (N.Y.)*, **118**, 113.
118. New Asian Dengue Held as Peril to U.S. Gulf States (1964): *Antibiot. News*, **1**, 3 (Nov. 25).
119. COOPER, W. C., GREEN, I. J., and FRESH, J. W. (1964): Laboratory Infection with Louping-ill Virus: A Case Study, *Brit. med. J.*, **ii**, 1627.
120. NELSON, E. R., and BIERMAN, H. R. (1964): Dengue Fever: A Thrombocytopenic Disease? *J. Amer. med. Ass.*, **190**, 99.
121. FAMA, P. G., PATON, W. B., and BOSTOCK, M. I. (1964): Thrombocytopenic Purpura Complicating Mumps, *Brit. med. J.*, **ii**, 1244.
122. SVENNINGSEN, N. W. (1965): Thrombocytopenia after Rubella, *Acta paediat. (Uppsala)*, **54**, 97.
123. CLARKE, B. F., and DAVIES, S. H. (1964): Severe Thrombocytopenia in Infectious Mononucleosis, *Amer. J. med. Sci.*, **248**, 703.
124. REIMANN, H. A. (1924): The Blood Platelets in Pneumococcus Infection, *J. exp. Med.*, **40**, 553.
- REIMANN, H. A., and JULIANELLE, L. A. (1925): The Production of Purpura by Derivatives of Pneumococcus, *ibid*, **43**, 97.
125. REIMANN, H. A., LU, G. Y. C., and YANG, C. S. (1929): The Blood Platelets in Typhus Fever, *Arch. Path.*, **7**, 640.
126. HOLT, G. W. (1965): Epidemic Neuro-myasthenia: The Sporadic Form, *Amer. J. med. Sci.*, **249**, 98.
127. A New Dermatoses? (1964): Lead. Art, *Brit. med. J.*, **ii**, 1547.
128. WARIN, R. P., et al. (1964): Outbreaks of a Papulo-Vesicular Exanthem on the Hands and Feet ("Summer-term Blains"), *Brit. med. J.*, **i**, 1413.
- 128a. PERALTA, P. H., SHELOKOV, A., and BRODY, J. A. (1965): Chagres Virus: A New Human Isolate from Panama, *Amer. J. trop. Med. Hyg.*, **14**, 146.
129. BARNES, M. G., and BRAINERD, H. (1964): Pneumonitis with Alveolar-Capillary Block in a Cattle Rancher Exposed to Epizootic Bovine Abortion, *New Engl. J. Med.*, **271**, 981.
130. RASK-NIELSEN, R. (1964): Coombs-positive Hemolytic Anemia and Generalized Amyloidosis in Mice Following Transmission of Subcellular Leukemic Material, *Proc. Soc. exp. Biol. (N.Y.)*, **116**, 1154.
131. OROSZLAN, S., and RICH, M. A. (1964): Human Wart Virus: In vitro Cultivation, *Science*, **146**, 531.

132. SMITH, T. J., MCKINNEY, R. W., and SAWYER, W. D. (1964): Isolation of Venezuelan Equine Encephalomyelitis Virus by Bone Marrow Culture, *Proc. Soc. exp. Biol. Med.*, **117**, 271.
133. MILLER, J. D. (1964): Viral Diseases as Hospital Acquired Infections, Program. Amer. Coll. Phys. Oct. 8, p. 11.
134. MEYERS, P. A., and MAY, R. (1964): Virus Transmission in Enemas, *Amer. J. Roentgenol.*, **91**, 864.
135. BLATTNER, R. J. (1964): Possible Role of Virus Infection in Sudden Unexpected Death, *J. Pediat.*, **65**, 631.
136. "Slow Viruses" Bring Sure Diseases to Animals; Effect on Man Suspected (1964): *Antibiot. News*, **1**, 8.
137. FRUITSTONE, M. J., WADDELL, G. H., and SIGEL, M. M. (1964): An Interferon Produced in Response to Infection by Herpes Simplex Virus, *Proc. Soc. exp. Biol. (N.Y.)*, **117**, 804.
138. WHELOCK, E. F. (1964): Interferon in Dermal Crusts of Human Vaccinia Virus Vaccination. Possible Explanation of Relative Benignity of Variolation Smallpox, *Proc. Soc. exp. Biol. (N.Y.)*, **117**, 650.
139. CAMERMANN, N., and TROTTER, J. (1964): 5-Iodo-2'-deoxyuridine: Relation of Structure to its Antiviral Activity, *Science*, **144**, 1348.
140. FORCE, E. E., and STEWART, R. C. (1964): Effect of 5-Iodo-2'-Deoxyuridine on Multiplication of Rous Sarcoma in vitro, *Proc. Soc. exp. Biol. (N.Y.)*, **116**, 803.
141. FURUSAWA, E., FURUSAWA, S., and CUTTING, W. (1965): Further Studies of Drug Combinations for Complete Cure of DNA Virus Infection in Cultured Cells, *Proc. Soc. exp. Biol. (N.Y.)*, **118**, 394.
142. Second Look at First Effective Antiviral Agent (1964): Med. News, *J. Amer. med. Ass.*, **189**, 38.
143. JUEL-JENSON, B. E., and MACCALLUM, F. O. (1964): Treatment of Herpes Simplex Lesion of the Face with Idoxuridine: Results of a Double-blind Controlled Study, *Brit. med. J.*, **ii**, 987.
144. Viral Infections (1964): Med. News, *J. Amer. med. Ass.*, **190**, 41.
145. MACCALLUM, D. D., JOHNSTON, E. N. M., and BAJA, B. H. (1964): 5 Iodo-2'-Deoxyuridine in the Treatment of Herpes Zoster, *Brit. J. Derm.*, **76**, 459.
146. IVE, F. A. (1964): A Trial of 5-Iodo-2'-Deoxyuridine in Herpes Simplex, *Brit. J. Derm.*, **76**, 463.
147. SOWA, S., and SOWA, J. (1964): Attempted Therapy of Trachoma with 5-Iodo-2'-Deoxyuridine, *Brit. med. J.*, **ii**, 989.
148. MASSAB, H. F., and COCHRAN, R. W. (1964): Influence of 5-Fluorodeoxyuridine on Growth Characteristics of Rubella Virus, *Proc. Soc. exp. Biol. (N.Y.)*, **177**, 410.
149. DAVIES, W. L., et al. (1964): Antiviral Activity of 1-Admantanamine (Amantadine), *Science*, **144**, 862.
150. MASSAB, H. F., and COCHRAN, K. W. (1964): Rubella Virus: Inhibition in Vitro by Amantadin Hydrochloride, *Science*, **145**, 1443.
151. "Viractin" Against Upper Respiratory Infections (1964): Lead. Art, *Brit. med. J.*, **ii**, 1482.
152. MITSUI, Y., et al. (1964): Trachoma: Its Treatment with a Long-Acting Sulfonamide Administered Orally, *Amer. J. trop. Med. Hyg.*, **13**, 488.
153. GRAYSTON, J. T., et al. (1964): Prevention of Trachoma with Vaccine, *Arch. environm. Hlth.*, **8**, 518.
154. ARTENSTEIN, M. S., and DEMIS, D. J. (1964): Recent Advances in the Diagnosis and Treatment of Viral Diseases of the Skin, *New Engl. J. Med.*, **270**, 1101.
155. Methisazone Disappointing in South Africa (1965): Internat. Comments, *J. Amer. med. Ass.*, **191**, 612.
156. Promise and Caution in Leukemia (1964): *Mod. Med.*, **32**, 26.
157. Viruses Could Trigger Cancer, but might not be a Primary Cause (1964): Med. News, *J. Amer. med. Ass.*, **190**, 30.
158. INMAN, D. R., WOODS, D. A., and NEGRONI, G. (1964): Viruses in Leukemia, *Brit. med. J.*, **i**, 929.
159. MURPHY, W. H., FURTADO, D., and PLATA, E. (1964): Possible Association between Leukemia in Children and Virus-like Agents, *J. Amer. med. Ass.*, **191**, 122.
160. PHILLIPS, C. F., et al. (1965): Failure to Isolate Viral Agents from Bone-marrow of Children with Acute Leukemia, *Brit. med. J.*, **i**, 286.
161. Infective Agents in Human Leukaemia (1965): Lead. Art, *Brit. med. J.*, **i**, 286.
162. MILLER, R. W. (1964): Radiation, Chromosomes and Viruses in the Etiology of Leukemia, *New Engl. J. Med.*, **271**, 30.
163. Viruses and Leukemia (1964): Leading Articles, *Lancet*, **i**, 1259.
164. WHELOCK, E. F., and DINGLE, J. H. (1964): Observations on the Repeated Administration of Viruses to a Patient with Acute Leukemia, *New Engl. J. Med.*, **271**, 645.
165. BODEY, J. P., et al. (1964): Use of Gamma-globulin in Infection in Acute-Leukemia Patients, *J. Amer. med. Ass.*, **190**, 1099.
166. BELL, T. M., et al. (1964): Isolation of a Reovirus from a Case of Burkitt's Lymphoma, *Brit. med. J.*, **i**, 1212.
167. SORENSEN, G. D. (1965): Virus-like Particles in Myeloma Cells of Man, *Proc. Soc. exp. Biol. (N.Y.)*, **118**, 250.
168. HILLEMANN, M. R. (1964): Prospects for the Role of Viruses in Human Malignancy, *Health Lab. Sci.*, **i**, 70.
169. ANDREWES, C. H. (1964): Tumour-Viruses and Virus-Tumours, *Brit. med. J.*, **i**, 653.
170. GIRARDI, A. J., HILLEMANN, M. R., and ZWICKY, R. E. (1964): Tests in Hamsters for Oncogenic Quality of Ordinary Viruses Including Adenovirus Type 7, *Proc. Soc. exp. Biol. (N.Y.)*, **115**, 1141.
- LARSON, V. M., et al. (1965): Studies of Oncology of Adenovirus Type 7 Viruses in Hamsters, *ibid*, **118**, 15.
171. RAPP, F., MELNICK, J. L., and KITAHARA, T. (1965): Tumor and Virus Antigens of Simian Virus 40: Differential Inhibition of Synthesis by Cytosine Arabinoside, *Science*, **147**, 625.

172. GOLDNER, H., *et al.* (1964): Interruption of SV40 Virus Tumorigenesis Using Irradiated Homologous Tumor Antigen, *Proc. Soc. exp. Biol. (N.Y.)*, **117**, 851.
173. GERBER, P. (1964): Virogenic Hamster Tumor Cells: Induction of Virus Synthesis, *Science*, **145**, 833.
174. SMITH, R. O., and MELNICK, J. L. (1964): Adenovirus-like Particles from Cancers Induced by Adenovirus-12 but Free of Infectious Virus, *Science*, **145**, 1190.
175. GIRARDI, A. J., LARSON, V. M., and HILLMAN, M. R. (1965): Further Tests in Hamsters for Oncogenic Quality of Ordinary Viruses and Mycoplasma, with Correlative Review, *Proc. Soc. exp. Biol. (N.Y.)*, **118**, 173.
176. MCBRIDE, W. D., and WIERNER, A. (1964): *In vitro* Transformation of Hamster Kidney Cells by Human Adenovirus Type 12, *Proc. Soc. exp. Biol. (N.Y.)*, **115**, 870.
177. EDDY, B. E., GRUBBS, G. E., and YOUNG, R. D. (1964): Tumor Immunity in Hamsters Infected with Adenovirus Type 12 or Simian Virus 40, *Proc. Soc. exp. Biol. (N.Y.)*, **117**, 575.
178. CRAMBLETT, H. G., and EDMOND, E. W. (1964): Adenovirus Type 12 Infection, *J. Amer. med. Ass.*, **188**, 1086.
179. GIRARDI, A. J., and HILLEMANN, M. R. (1964): Host Virus Relationships in Hamsters Inoculated with SV40 Virus During the Neonatal Period, *Proc. Soc. exp. Biol. (N.Y.)*, **116**, 723.
180. Tumours Caused by Viruses (1964): Lead. *Art. Brit. med. J.*, **i**, 647.
181. MEDES, G., and REIMANN, S. P. (1963): Normal Growth and Cancer, pp. 194 to 254. Philadelphia and Montreal: J. B. Lipincott.
182. A Rise in Tuberculosis (1964): *Mod. Med.*, **32**, 54.
183. MENZIN, A. W. (1964): Current Immunization Methods and Materials, *Arch. intern. Med.*, **107**, 409.
184. DUBOS, R. (1964): Acquired Immunity to Tuberculosis, *Amer. Rev. resp. Dis.*, **90**, 505.
185. Eradication of Tuberculosis: A Problem in Epidemiologicopedics (1965): Edit. *J. Amer. med. Ass.*, **191**, 492.
186. TODD, R. M., and NEVILLE, M. B. (1964): Sequelae of Tuberculous Meningitis, *Arch. Dis. Childh.*, **39**, 213.
187. HOBBS, G. L. (1965): Primary Drug Resistance: II. Continuing Study of Tubercle Bacilli in Veteran Population within the U.S., *Amer. Rev. resp. Dis.*, **91**, 30.
188. KLINENBERG, J. R., GRIMLEY, P. M., and SEGMILLER, G. E. (1965): Destructive Polyarthritides Due to a Photochromogenic Mycobacterium, *New Engl. J. Med.*, **272**, 190.
189. JOHNSON, W. W., and SMITH, D. T. (1964): Cross Reactions with Tuberculin on Guinea Pigs with Single and Double Experimental Infections with Mycobacteria, *Proc. Soc. exp. Biol. (N.Y.)*, **116**, 1024.
190. WALKER, S. H., and PATRON, L. R. (1964): Unclassified Mycobacterial Infections in Children, *Amer. J. Dis. Childh.*, **108**, 460.
191. REIMANN, H. A., and MA, P. P. C. (1965): Dissociation of M. Tuberculosis and Atypical Mycobacteria, *Amer. Rev. resp. Dis.*, in press.
192. Leprosy in the Netherlands (1964): *Genees. Gids.*, **42**, 375.
193. PETIT, J. H. S., and REES, R. J. W. (1964): Sulfone Resistance in Leprosy, *Lancet*, **i**, 673.
194. SHEPARD, C. C. (1964): Capreomycin: Activity Against Experimental Infection with Mycobacterium Leprae, *Science*, **146**, 403.
195. VAKIL, B. J., MEHTA, A. J., and TULPUL, T. (1964): Recurrent Tetanus, *Postgrad. med. J.*, **40**, 601.
196. SCUDDER, P. A., and MCCARROLL, J. R. (1964): Current Status of Tetanus Control. Importance of Human Tetanus-Immune Globulin, *J. Amer. med. Ass.*, **188**, 625.
197. ECKMAN, L. (1964): Active and Passive Tetanus Immunization, *New Engl. J. Med.*, **40**, 601.
198. SMITH, J. W. G. (1964): Penicillin in the Prevention of Tetanus, *Brit. med. J.*, **i**, 1293.
199. PASCALE, L., *et al.* (1964): Treatment of Tetanus with Hyperbaric Oxygenation, *Amer. med. Ass.*, **189**, 408.
200. GOTSCHMAN, M. S., and WHITBY, J. L. (1964): Respiratory Infection Following Tracheostomy, *Thorax*, **19**, 89.
201. MEADE, J. N. (1964): Tracheostomy—Its Complications and Their Management: Study of 212 Cases, *New Engl. J. Med.*, **265**, 519.
202. BERGGREN, R. B., *et al.* (1964): Clostridial Myositis from Injections, *J. Amer. med. Ass.*, **188**, 1044.
203. SEGRE, D. (1964): Cytopathic Effects of Normally Non-Cytopathogenic Viruses in Tissue Cultures Held Under Increased Oxygen Pressure, *Proc. Soc. exp. Biol. (N.Y.)*, **117**, 577.
204. KOHLER, P. F. (1964): Hospital Salmonellosis, *J. Amer. med. Ass.*, **189**, 6.
205. BILLE, B. T., MELLBRIN, F., and NORDBRING, A. (1964): An Extensive Outbreak of Gastroenteritis Caused by Salmonella Newport. Some Observations on 745 Known Cases, *Acta. med. scand.*, **175**, 557.
206. ASH, I., *et al.* (1964): Outbreak of Typhoid Fever Connected with Corned Beef, *Brit. med. J.*, **i**, 1474.
207. SHARP, J. C. M., BROWN, P. P., and SANGSTER, G. (1964): Outbreak of Paratyphoid in the Edinburgh Area, *Brit. med. J.*, **i**, 1282.
208. UWAYDAH, M., and SHAMMA'A, M. (1964): The Treatment of Typhoid Fever with Ampicillin, *Lancet*, **i**, 1242.
209. CHRISTIE, A. B. (1964): Treatment of Typhoid Carriers with Ampicillin, *Brit. med. J.*, **i**, 1609.
210. HEINEMANN, H. S., *et al.* (1964): Hodgkin's Disease and *Salmonella typhimurium* Infection, *J. Amer. med. Ass.*, **188**, 632.
211. Salmonella Surveillance, Comm. Dis. Center. U.S. Depart. H. E. and W. No. 27, (July 27) 1964.
212. Shigella Vaccine Ready for Clinical Trial (1964): *Antibiot. News*, **i**, 1.
213. BORIS, M., *et al.* (1964): Escherichia Coli Gastroenteritis, *Pediatrics*, **33**, 18.
214. ROZANSKY, R., *et al.* (1964): Enteropathogenic Esch. coli Infection in Infants during the Period from 1957 to 1962, *J. Pediat.*, **65**, 521.

215. Hospital Infections with *Pseudomonas Pyocyanea*, Lead. Art. (1964): *Brit. med. J.*, ii, 1019.
216. JACOBS, J. (1964): The Investigation of an Outbreak of *Pseudomonas Pyocyanea* Infection in a Pediatric Unit, *Postgrad. med. J.*, **40**, 590.
217. MAIZTEGUI, J. I., *et al.* (1965): Bacteremia Due to Gram-Negative Rods, *New Engl. J. Med.*, **272**, 222.
218. Growth Rate of Bacteria (1964): *Med. News, J. Amer. med. Ass.*, **190**, 33.
219. MATZ, M. H., and BRUGSCH, H. G. (1964): Anthrax in Massachusetts: 1943 Through 1962, *J. Amer. med. Ass.*, **188**, 633.
220. Anthrax-Ohio (1964): Morbidity and Mortality. Weekly Report, U.S. Dept. H. E., and W., **13**, 117.
221. Outbreak of Anthrax in Northwest Territories (1964): *Med. Serv. J. Can.*, **20**, 531.
222. KOHOUT, E., SEHAT, A., and ASHRAF, M. (1964): Anthrax: A Continuous Problem in Southwest Iran, *Amer. J. med. Sci.*, **247**, 565.
223. PHILLIPS, R. A. (1964): Water and Electrolyte Losses in Cholera, *Fed. Proc.*, **23**, 705.
224. REIMANN, H. A., *et al.* (1946): Asiatic Cholera. Clinical Study and Experimental Therapy with Streptomycin, *Amer. J. trop. Med.*, **26**, 631.
225. DEBONO, J. E. (1964): Brucellosis Simulating Acute Anterior Poliomyelitis, *Lancet*, i, 1132.
226. SPINK, W. W. (1964): Chronic Suppuration with Brucellosis, *Amer. J. med. Sci.*, **247**, 129.
227. Plague Outbreak in Madras (1964): *Brit. Med. News*, Apr. 17.
228. FEELEY, E. J., and KRIZ, J. J. (1965): Plague Meningitis in an American Serviceman, *J. Amer. med. Ass.*, **191**, 412.
229. WEIL, M. H., SHUBIN, H., and BIDDLE, M. (1964): Shock Caused by Gram-Negative Organisms, *Ann. intern. Med.*, **60**, 384.
229. "Endotoxin Shock" (1964): Editorial, *J. Amer. med. Ass.*, **190**, 847.
230. OVERHOTT, E. L., and GRAMES, G. M. (1964): Gram-Negative Septicemia, *Milit. Med.*, **129**, 181.
231. NELSON, J. D., HEMPSTEAD, B., TANAKA, R., and PAULS, F. P. (1964): Fluorescent Antibody Diagnosis of Infections, *J. Amer. med. Ass.*, **188**, 1121.
232. FEINSTEIN, A. R., *et al.* (1965): Prophylaxis of Recurrent Rheumatic Fever, Ineffectiveness of Intermittent "Therapeutic" Oral Penicillin, *J. Amer. med. Ass.*, **191**, 451.
233. BREESE, B. B., DISNEY, F. A., and TALPEY, W. B. (1964): Streptococcal Infection in Children, *Amer. J. Dis. Child*, **107**, 232.
234. MICHAEL, T. M., MICHAEL, J. B., and MASSELL, B. F. (1964): Production of Penicillinase by Staphylococci in the Throat, *Amer. J. med. Sci.*, **248**, 152.
235. KUNDSIN, R. B., and MILLER, J. M. (1964): Significance of the Staphylococcus Aureus Carrier State in the Treatment of Disease Due to Group A Streptococci, *New Engl. J. Med.*, **271**, 1395.
236. STOLLERMAN, G. A. (1964): Sore Throat—A Diagnostic and Therapeutic Dilemma, *J. Amer. med. Ass.*, **189**, 145.
237. FORDHAM, C. C., *et al.* (1964): Polyarteritis and Acute Post-Streptococcal Glomerulonephritis, *Ann. intern. Med.*, **61**, 89.
238. Follow-up of an Epidemic (1964): *Mod. Med.*, **32**, 51.
239. EICKHOFF, T. C., *et al.* (1964): Neonatal Sepsis and Other Infections Due to Group B Beta-Hemolytic Streptococci, *New Engl. J. Med.*, **271**, 1221.
240. KARAKAWA, W. W., ROTTA, J., and KRAUSE, R. M. (1965): Detection of M Protein in Colonies of Streptococcal L Forms by Immunofluorescence, *Proc. Soc. exp. Biol. (N.Y.)*, **118**, 198.
- 240a. MATTMAN, L. H., and MATTMAN, R. E. (1965): L Forms of Streptococcus Fecalis in Septicemia, *Arch. intern. Med.*, **115**, 315.
241. SASLAW, M. S., and VIETA, A. G. (1964): Limits to Rheumatic Fever Prevention, *Pediatrics*, **64**, 552.
242. MASSELL, B. F., AMEZCUA, F., and PELARGONIO, S. (1964): Evolving Picture of Rheumatic Fever. Data from 40 Years at the House of the Good Samaritan, *J. Amer. med. Ass.*, **118**, 287.
243. ORLOVSKAIA, G. W. (1964): Development of Pattern of Tissue Changes in Rheumatic Heart, *Vop. Revm.*, **4**, 26.
244. Combined Rheumatic Fever Study Group (1965): A Comparison of Short-term, Intensive Prednisone and Acetylsalicylic Acid Therapy in the Treatment of Acute Rheumatic Fever, *New Engl. J. Med.*, **272**, 63.
245. RAMMELKAMP, C. H., MORTIMER, E. A., and WOLINSKY, E. (1964): Transmission of Streptococcal and Staphylococcal Infections, *Ann. intern. Med.*, **60**, 753.
246. EHRENKRANZ, N. J. (1964): Person to Person Transmission of Staphylococcus Aureus, *New Engl. J. Med.*, **271**, 252.
247. BULLOCK, W. E., *et al.* (1964): A Staphylococcal Isolation Service. Epidemiologic and Clinical Studies Over One Year, *Ann. intern. Med.*, **60**, 777.
248. KISLACK, J. W., EICKHOFF, T. C., and FINLAND, M. (1964): Hospital Acquired Infection and Antibiotic Usage in the Boston City Hospital—January, 1964, *New Engl. J. Med.*, **271**, 834.
249. JENSEN, K., and LASSEN, H. C. A. (1964): Fulminating Staphylococcal Infections Treated with Fucidin and Penicillin or Semisynthetic Penicillin, *Ann. intern. Med.*, **60**, 790.
250. BORIS, M., *et al.* (1964): Bacterial Interference: Protection of Adults Against Nasal Staphylococcus Infection after Colonization with Heterologous *S. aureus* Strain, *Amer. J. Dis. Child*, **108**, 252.
- 250a. ZYSKIND, J. W., PATTEE, P. A., and LACHE, M. (1965): Staphylolytic Substance from a Species of *Pseudomonas*, *Science*, **147**, 1458.
251. KUNDSIN, R. B., WALTER, C. W., and MORIN, P. (1964): Staphylococcus Aureus C-18: Agent of Nosocomial Infections, *Science*, **145**, 1322.
252. AUSTRIAN, R., and GOLD, J. (1964): Pneumococcal Bacteremia with Especial Reference to Bacteremic Pneumococcal Pneumonia, *Ann. intern. Med.*, **60**, 759.
253. WILSON, F. M., and LERNER, A. M. (1964): Etiology and Mortality of Purulent Meningitis at the Detroit Receiving Hospital, *New Engl. J. Med.*, **271**, 1235.
254. SOCIA, J. L., DiBENEDETTO, R., and CROCCO, J. (1964): Klebsiella Pneumoniae Meningitis.

- Report of a Case and Review of the Literature, *Arch. intern. Med.*, **113**, 569.
255. FLORDE, J. J., GARCIA, M., and PETERSDORF, R. G. (1964): Studies on the Pathogenesis of Meningitis: IV. Penicillin Levels in the Cerebrospinal Fluid in Experimental Meningitis, *J. Lab. clin. Med.*, **64**, 960.
 256. EICKHOFF, T. C., and FINLAND, M. (1965): Changing Susceptibility of Meningococci to Antimicrobial Agents, *New Engl. J. Med.*, **274**, 395.
 257. PASCOE, D. J., and LUFKIN, C. D. (1964): Meningococcal Disease Due to a Sulfadiazine Resistant Strain, *Pediatrics*, **34**, 124.
 258. SPANGLER, A. S., et al. (1964): Syphilis with a Negative Blood Test Reaction, *J. Amer. med. Ass.*, **189**, 87.
 259. KAIL, F., and STEPPERT, A. (1964): Cases of Syphilis Detected by the VDRL Test in Blood Donors of the Austrian Army During the Years 1960 to 1963, *Wien. klin. Wschr.*, **76**, 605.
 260. The Spread of Gonorrhoea (1964): Leading Articles, *Lancet*, **ii**, 511.
 261. PARISER, H., FARMER, A. D., and MARINO, A. F. (1964): Asymptomatic Gonorrhea in Men, *Sth. med. J. (Bgham., Ala.)*, **57**, 688.
 262. Detection of Gonorrhea Antibody Obscured in Meningitis Carriers, (1964), *Antibiot. News*, **1**, 5.
 263. SHEPARD, M. C., et al. (1964): Possible Role of T-Strain Mycoplasma in Nongonococcal Urethritis, *J. Amer. med. Ass.*, **188**, 729.
 264. MORTON, R. S., GILLESPIE, E. H., and WILSON, M. A. (1964): Virus Culture Studies in Non-Gonococcal Urethritis, *J. clin. Path.*, **17**, 114.
 265. KELLOGG, D. S., and DEACON, W. E. (1964): A New Rapid Immunofluorescent Staining Technique for Identification of Treponema pallidum and Neisseria Gonorrhoeae, *Proc. Soc. exp. Biol. (N.Y.)*, **115**, 963.
 266. HESS, E. V., HUNTER, D. K., and ZIFF, M. (1965): Gonococcal Antibodies in Acute Arthritis, *J. Amer. med. Ass.*, **191**, 531.
 267. TIEDEMAN, J. H., HACKNEY, J. F., and PRICE, E. V. (1965): Acute Gonorrheal Urethritis in Men, *J. Amer. med. Ass.*, **191**, 89.
 268. BAKER, R. D. (1964): Histoplasmosis in Routine Autopsies, *Amer. J. clin. Path.*, **41**, 457.
 269. MURRAY, J. F., and HOWARD, D. (1964): Laboratory-Acquired Histoplasmosis, *Amer. Rev. resp. Dis.*, **89**, 631.
 270. WOODS, L. P., TINSLEY, E. A., and DIVELEY, W. L. (1964): Sputum Diagnosis of Histoplasmosis, *J. thorac. cardiovasc. Surg.*, **48**, 761.
 271. Formaldehyde Flushes Fields Harboring Histoplasma (1964): *Antibiot. News*, **1**, 8.
 272. FURCOLOW, M. L. (1965): Environmental Aspects of Histoplasmosis, *Arch. environm. Hlth.*, **10**, 4.
 273. Histoplasmosis Co-operative Study, V.A.-Armed Forces Co-operative Study on Histoplasmosis, *Amer. Rev. resp. Dis.*, **89**, 641.
 274. STOKER, D. G. (1964): Histoplasmosis in Cyprus: Report of Two Cases, *Brit. med. J.*, **ii**, 793.
 275. MARINKELLE, C. J., and GROSE, E. (1965): Histoplasma Capsulatum from the Liver of a Bat in Colombia, *Science*, **147**, 1039.
 276. SOTGIU, G., and MAZZONI, A. (1965): Histoplasma Capsulatum: Occurrence in Soil from the Emilia-Romagna Region of Italy, *Science*, **147**, 624.
 277. LEZNOFF, A., et al. (1964): Histoplasmosis in Montreal during the Fall of 1963, with Observations on Erythema Multiforme, *Canad. med. Ass. J.*, **91**, 1154.
 278. SHIMA, S. (1964): Histoplasmin Sensitivity in Japan, *Dis. Chest.*, **46**, 692.
 279. COCKSHOT, W. P., and LUCAS, A. O. (1964): Histoplasmosis Duboisii, *Quart. J. Med.*, **33**, 223.
 280. DRIPS, W., and SMITH, C. E. (1964): Epidemiology of Coccidioidomycosis, A Contemporary Military Experience, *J. Amer. med. Ass.*, **190**, 1010.
 281. JOHNSON, J. E., et al. (1964): Laboratory-acquired Coccidioidomycosis, A Report of 210 Cases, *Ann. intern. Med.*, **60**, 941.
 282. CARBONE, P. P., et al. (1964): Secondary Aspergillosis, *Ann. intern. Med.*, **60**, 556.
 283. KOZINN, P. J., CAROLINE, L., and TASHJIAN, C. L. (1964): Conjunctiva Contains Factor Inhibiting Growth of Candida albicans, *Science*, **146**, 1479.
 284. PROCKNOW, J. J., et al. (1965): Cryptococcal Hepatitis Presenting as a Surgical Emergency, *J. Amer. med. Ass.*, **191**, 269.
 285. Malaria Surveillance, 1963 Annual Summary, Comm. Dis. Center, Atlanta, Ga.
 286. COLLINS, W. F., JEFFERY, G. M., and SKINNER, J. C. (1964): Fluorescent Antibody Studies in Human Malaria, *Amer. J. trop. Med. Hyg.*, **13**, 1; *ibid.*, **13**, 256; *ibid.*, **13**, 776.
 287. VOLLER, A., and WILSON, H. (1964): Immunological Aspects of Population under Prophylaxis against Malaria, *Brit. med. J.*, **ii**, 551.
 288. Long-Term Protection against Malaria (1964): *Mod. Med.*, Aug. 3, p. 54.
 289. MOST H. (1965): The Pendulum in Malaria Chemotherapy: From Quinine to Chloroquine and Back to Quinine? *Milit. Med.*, **129**, 587.
 290. Setback in Malaria Battle (1964): *Mod. Med.*, Aug. 3, p. 54.
 291. LEGTERS, L. G., et al. (1965): Apparent Refractoriness of Chloroquine, Pyrimethamine and Quinine in Strains of Plasmodium Falciparum from Vietnam, *Milit. Med.*, **130**, 168.
 292. CAHILL, K. M. (1964): Leishmaniasis in the Sudan Republic, *Amer. J. trop. Med. Hyg.*, **13**, 794.
 293. CARPENTER, C. B., MOZLEY, P. D., and LEWIS, N. G. (1964): Schistosomiasis Japanica Involvement of the Female Genital Tract, *J. Amer. med. Ass.*, **188**, 647.
 294. GOLDBERG, H. S., BLENDEEN, D. C., and LOGUE, J. T. (1965): Leptospirosis in Random and Select Populations, *Arch. Environm. Hlth.*, **10**, 21.
 295. MAGATH, T. B. (1965): Ecchinococcus Multicellularis in a Beef Cow from the Middle West, *Science*, **147**, 632.
 296. KEAN, B. H., and HOSKINS, D. W. (1964): Treatment of Trichinosis with Thiabendazole, *J. Amer. med. Ass.*, **190**, 852.
 297. LABZOFFSKY, N. A., et al. (1964): Fluorescent Test for Trichinosis, *Canad. med. Ass. J.*, **90**, 920.

298. Letter, Eli Lilly Co., Sept. 4, 1964.
299. A Change in the Urine (1964): *Mod. Med.*, **32**, 40.
300. SANFORD, J. P. (1964): Hospital Acquired Urinary-Tract Infections, *Ann. intern. Med.*, **60**, 903.
301. Bladder has Own Defenses against Bacterial Invaders (1964): *Med. World News*, **5**, 26.
302. COX, C. E., and HINMAN, F. (1965): Retention Catheterization and the Bladder Defense Mechanism, *J. Amer. med. Ass.*, **191**, 171.
303. PERCIVAL, A., BRUMFITT, W., and DELOUVOIS, J. (1964): Serum-Antibody Level as an Indication of Clinically Inapparent Pyelonephritis, *Lancet*, **ii**, 1027.
304. RIFKIND, D., *et al.* (1964): Infectious Diseases Associated with Renal Homotransplantation, *J. Amer. med. Ass.*, **189**, 397.
305. KALMANSON, G. M., and GUZE, L. B. (1964): Role of Protoplasts in Pathogenesis of Pyelonephritis, *J. Amer. med. Ass.*, **190**, 1107.
306. SEELEY, S. F. (1964): Influence of Ultraviolet Light on Post-operative Infection, Editorial, *J. Amer. med. Ass.*, **189**, 574. See also *Ann. Surg.* 1964: **160**, No. 2 Suppl., pp. 9-192.
307. WOOD, P. H. (1964): Sickness and Settlement. Disease as a Factor in the Early Colonization of New England, *The Pharos of Alpha Omega Alpha Soc.*, **27**, 98.
308. MILLER, J. F. A. P. (1964): The Thymus and the Development of Immunologic Responsiveness, *Science*, **144**, 1544.
309. Electronmicroscopy, Fifth International Congress, S. S. Breese, Edit., Vol. 2, New York and London: Academic Press.
310. REIMANN, H. A., (1965): Microbic Phagocytosis by Enteric Epithelial Cells, *J. Amer. med. Ass.*, **192**, 1130.
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