ANNUAL REVIEW

Infectious Diseases Annual review of significant publications

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Introduction

The changing nature and diminished incidence of infectious diseases chiefly as the results of modern sanitation, immunization and therapy, were reviewed by Gsell.¹ As one example of a change, pneumonia, the leading subject in the 1937 Review of this series, occupied nine pages with thirty-six references. In this issue, the subject merited one-half page and seven references.

As usual in recent years, antimicrobial drugs and their clinical application and viral diseases received the most attention in 1968. Many new drugs were introduced. Increased recognition revealed more untoward effects of antibacterial therapy, of vaccination, of the use of γ -globulin and of immunosuppressive procedures. Pandemic influenza caused by a virus different antigenically from older strains caused much concern and a rush to prepare a specific vaccine. Immunizing methods against other viral diseases, especially rubella, rubeola and mumps advanced in effectiveness. Antiviral drugs are under investigation. Virus or virus-like particles in various tissues raised the question whether they were actually pathogenic, latent or commensal. Several methods for the rapid identification of microbes and infections by automated and fluorescent procedures were proposed.

Antimicrobial drugs

Many names were coined for newly prepared antimicrobial drugs some of which are no better than ones now available. Among them are lydimycin, nebramycin, rifampin, kalofungin, kitasamycin, minocycline, veracillin, troleandomycin, versapen, puromycin and fusidate. The known polypeptide antimicrobics probably represent only a few of many others still undiscovered.² With twenty-six letters in the alphabet, opportunity is limitless for new names, euphonic or not.

Cephaloridine eradicated pneumococci, strepto-

No reprints of this article are available.

cocci, *E. coli* and *Proteus mirabilis*, but was irregularly active against *Klebsiella*. During therapy, superinfection with Gram-negative bacilli occasionally caused death. The drug is potentially nephrotoxic and neurotoxic,³ but can be used when cephalothin is not tolerated. It may cause a reaction in penicillin-sensitive patients.⁴ Neither cephaloridine nor cephalothin was active against many strains of enterococci, indole-positive *Proteus* and *Pseudomonas*.⁵ Large dosage of cephaloridine failed in three instances of *H. influenzae* meningitis.⁶ Cephalothin may be used for endocarditis in penicillin-sensitive patients.⁷

Lincomycin was as effective as penicillin for pneumococcal pneumonia, but they should not be given together. The cocci may become resistant to lincomycin.⁸ Orally administered ampicillin was better than neomycin for treating shigellosis.⁹ Neomycin instilled into wounds or given prophylactically failed to reduce the rate of complications or to prevent infections.¹⁰ Hetacillin controlled some bacterial respiratory tract infections, twenty-eight of forty urinary tract infections and one instance of enterococcal endocarditis. Allergic reactions were frequent.¹¹ Most of 100 strains of *K. pneumoniae* and *P. vulgaris* were sensitive to gentamicin.¹² Carbenicillin probably controlled septicemia and meningitis caused by *Pseudomonas* in several patients.¹³ Cephaloglycin, an analogue of cephalosporin, was active against Gram-positive cocci and Gram-negative bacilli. It was used successfully for the treatment of urinary tract infections.¹⁴ Colistimethate (Climycin) had no advantage over polymyxin B and is unavailable for intravenous use for severe infection with *Pseudomonas*.¹⁵ Reports in the *American Journal of the Medical Sciences* of October do not favor the general use of rifampin because of the frequency of bacterial resistance to it. It was used successfully in treating tuberculosis¹⁶ and gonorrhea.¹⁷

Meningitis from *H. influenzae* relapsed when oral therapy replaced parenteral injection of ampicillin.¹⁸ Intramuscular and intravenous injection of anti-

microbic drugs effectively controlled pyogenic arthritis.^{18a} Intraarticular and intraspinal injections are unnecessary and may cause harm. It is important to place the drug in the infected tissue, not in the pus.

Thiabendazole was effective against ascariasis, trichinosis, uncinariasis and other helminthic diseases, but must be used cautiously when hepatic disease is present.¹⁹ Candidiasis and cryptococcosis responded to therapy with 5-fluorocytosine.²⁰ A new thiadiazol compound having forty-five numerals and letters in its name was highly active against bacteria and other parasites.²¹

A component of agar used in sensitivity tests interfered with the diffusion of polymyxin and some other drugs. Toxicity from polymyxin in patients may result from the binding of the drug to tissue.²² Host determinants of response to antimicrobial agents were discussed in a series of papers in the August 30, September 5 and 12 issues of the *New England Journal of Medicine*.

Variant forms of bacteria without cell walls that resemble Mycoplasmas appear in culture media especially during antimicrobial therapy. These may not be pathogenic, but are able to become so by reversion to the original form. They may account for relapsing and chronic infections and for failure of therapy.²³

Unwanted effects of antimicrobial therapy

Despite the great value of antimicrobial therapy, untoward effects occur oftener than are generally realized. It may be difficult to differentiate them from those caused by the disease under treatment. Harmful effects can be reduced by proper prescription of the drugs.

Amounts of 20×10^6 units or more of penicillin caused hemolytic anemia in two observed patients and in twelve other reported instances. All had received penicillin previously.²⁴ Huge dosage also causes neural disturbance, sometimes fatally. Allergic reactions in three patients followed inadvertent inhalation of small amounts of penicillin.²⁵ Allergic reactions occur in about 5% of treated adult patients especially those with a history of atopy. The risk of a fatal reaction is estimated as two in 100,000.²⁶ Penicillin-resistant hemolytic streptococci appeared in the throat of about 75% of children given penicillin prophylactically. The cocci disappeared when the drug was stopped.²⁷ Agranulocytosis and histiocytosis resulted from therapy with ampicillin.²⁸ Nephropathy followed therapy with 24 g of methicillin or from 20 to 60×10^6 units of penicillin in seven patients. All but one recovered.²⁹ In a hospital, methicillin-resistant staphylococci appeared in eighteen patients and infected fifteen of them.³⁰ Of twenty-five penicillin-sensitive patients treated with cephalothin, one had a fatal anaphylactic shock,

another had a severe shock but recovered, and thirteen had hemolytic anemia. Others had rashes, fever and serum sickness.³¹

Although tetracyclines occasionally are toxic in pregnant women, other women may be similarly harmed; men rarely are.³² Death in a patient with renal dysfunction was ascribed to the administration of 5.75 g of tetracycline intravenously during 5 days and 4 g orally for 2 days.³³ Neomycin, kanamycin, polymyxin, bacitracin and colistin may cause myasthenia, especially during renal failure by interfering with the release of acetylcholine from neural endings.³⁴ Even small amounts of kanamycin may be ototoxic.³⁵ Kanamycin, especially in large dosage for the treatment of gonorrhea may enhance the survival of *Treponema pallidum*.³⁶ Cardiac arrest in four patients followed rapid intravenous injection of 4 g of lincomycin.³⁷ Interstitial pneumonia and fibrosis followed prolonged therapy with nitrofurantoin.³⁸

Twenty-eight of thirty-eight patients treated with the usual doses of isoniazid had impaired memory during therapy. This hazard must be borne in mind when the drug is dispensed on a large scale for prophylaxis.³⁹ Chloroquine in therapeutic dosage may cause seizures and other neural disturbances.⁴⁰ Nitrofurantoin therapy for a month caused toxic hepatitis and bleeding.⁴¹ Further experience with the use of antimicrobials during renal failure indicated that gentamicin, nitrofurantoin, chloramphenicol and colistin all may be cumulative and require care in administration.⁴²

The normal flora of the throat, particularly hemolytic streptococci, inhibits the growth of other bacteria. Suppression of the flora by antimicrobial drugs allows the emergence and overgrowth of resistant microbes.⁴³ As compared with untreated patients, the fecal flora of those who received antimicrobial drugs showed many more Gram-negative bacilli. *Klebsiella* increased from 10 to 34%.⁴⁴ Hexachlorophene baths resulted in a replacement of staphylococci with *Pseudomonas* among infants.⁴⁵

Toxic, allergic and other adverse effects of antimicrobial therapy were outlined in the *Medical Letter on Drugs and Therapeutics* of September 20. Mounting expenditure on antimicrobials, vaccines and medical care is probably greater than the cost of simpler measures needed for environmental prophylaxis.⁴⁶ According to a veterinarian, the 'antibiotic orgy' prevalent in his field has reduced the beneficial effects of antimicrobials on the growth of live-stock and poultry and has populated them with resistant bacteria which may invade man.⁴⁷

Viral infections

Specific viral infections of the respiratory tract

Influenza A₂/Hong Kong (a-Aichi)/68 first observed

in Hong Kong in July 1968 may not have originated there. As in previous instances, multiple sources probably existed. The new strain, different enough antigenically, was not affected by vaccines available at the time. About one-third of members of a Congress in Tehran in September were mildly sick as were some residents of that city. Over-publicized warnings caused much apprehension, but the infection which spread widely in the world was not more serious than other minor viral infections of the respiratory tract in other years except for patients with chronic cardio-pulmonary or other chronic disease. Specific vaccine is now available but may be ineffective if another antigenic change follows.

In two reports in the *Journal of the American Medical Association* of March 25 1968, amantadine HCl given prophylactically reduced the incidence and severity of infection with the old strain influenza A₂ in inoculated volunteers, but impaired antibody production. Rimantadine gave similar results and may be of value also against herpes hominis and varicellar infection. Amantadine injected intraperitoneally into mice had no effect on suppressing infection nor on pulmonic lesions caused by inoculating influenza A₂/Jap/305 virus. Rimantadine lessened the severity of the lesions and the ability of the virus to spread to other mice.⁴⁸ Neither drug has been shown to prevent infection with the A₂/Hong Kong/68 strain.⁴⁹ Isoquinoline given prophylactically reduced the incidence of influenza A₂ in inoculated volunteers.⁵⁰

Inhaled, aerosolized, killed A₂ virus vaccine, as suggested years ago by Russian investigators was said to result in a 79% reduction of illness in inoculated volunteers. Side-reactions followed in 15%, and in 32% of those who received vaccine subcutaneously.⁵¹ Inhaled vaccine induced a greater amount of local antibody than subcutaneous inoculation.⁵² Purified vaccine, free from egg-derived substance and twice as potent antigenically as older forms can be made in large quantities.⁵³

Symptoms of the common cold followed the intranasal inoculation of influenza C virus in volunteers.⁵⁴ About 12% of colds were caused by newly recognized RNA-viruses different from the known myxoviruses.⁵⁵ Both influenza⁵⁶ and respiratory syncytial viral infections⁵⁷ can be identified in secretions in less than three hours by applying direct immunofluorescent technique.

Dogs are susceptible to experimental infection with influenza virus A₂ and B. They were asymptomatic, but antibody often persisted for months.⁵⁸ Inferentially, dogs like hogs may be a source or reservoir of infection.

Rhinoviral infections

As in previous studies, chilling failed to predispose

volunteers to colds from rhinoviral infections.⁵⁹ My own experience is otherwise, but perhaps chilling causes vasomotor rhinitis which plays a role in inducing infection. Eight more types of rhinovirus were added to the fifty-five already numbered.^{60, 61} Infections probably leave transient immunity. The same type virus never recurred in repeated illnesses of patients. In one victim, five different types caused successive infections during a year. Several types may be active at once.⁶⁰ Heterotypic antibody in groups of viruses raises hopes of preparing an effective polyvalent vaccine.⁶²

A rhinovirus derived from patients caused in apparent infection in chimpanzees and antibody appeared in others in contact with them.⁶³ Bovine rhinoviruses are widespread in cattle.⁶⁴

Respiratory syncytial virus was present during otitis media in twenty-two infants up to the 9th day. Bacterial invasion is a danger.⁶⁵ Application of the immunofluorescent technique provided diagnoses of RS infection within 2-7 days⁶⁶ or earlier⁶⁷ as compared with a month needed for older methods. The virus when grown at 26°C loses invasiveness and this may provide a basis for preparation of a vaccine. Infection itself, not the presence of neutralizing antibody, confers immunity.⁶⁷

Adenoviral infections

Adenoviruses mostly of types 1, 2, 3 and 5 were isolated from 296 patients, chiefly children with upper respiratory tract infection. Etiologic diagnosis usually was made within 8 days by tests showing viral cytopathic effects. The lowest isolation rates were in winter.⁶⁸ An outbreak of adenoviral pharyngoconjunctival fever apparently originated in an unchlorinated swimming-pool. The attack-rate was 65%. Transmission to ten families at home followed with a similar attack-rate for children.⁶⁹ Type 11 adenovirus was said to have caused acute hemorrhagic cystitis in eleven children. Specific antibody increased in each and virus was recovered in nine.⁷⁰

Specific live vaccine decreased the incidence of type 4 adenoviral infection in previously immunized and less so in non-immunized naval personnel. Viral pneumonias, however, were not reduced in incidence. A different agent may have been the cause,⁷¹ or vaccination failed to prevent severe infections.

According to editorial comment, 'the case for using live adenovirus vaccine is open to serious doubt', firstly because of its unproved value and secondly because of the potential ability of the virus to incite tumors.⁷² Neither methisazone nor trifluorothymidine had influence on the prevention or treatment of conjunctivitis experimentally induced with adenovirus type 3.⁷³

Respiratory tract infections in general

Extensive studies during 4 years among university students showed the common-cold-type illness to be the commonest and pharyngitis second in frequency. Rhinoviral disease predominated in autumn; influenza A₂ and B outbreaks in the spring of 3 years. Parainfluenza and herpes simplex viral infections were endemic. Pneumonia caused by *Mycoplasma pneumoniae* was commonest in the autumn of 1964. A similar incidence of infections recurred among military and industrial personnel.⁷⁴

Different viruses cause infections and epidemics among different age-groups and circumstances. The behavior and distribution of viral respiratory tract diseases is the same in tropical climates as elsewhere.⁷⁵ During surveillance among 2000 children with acute febrile disease, the virus isolation rate was 20%, as in other similar studies. Four successive seasonal waves during a year were associated respectively with entero-, myxo-, adeno- and RS viruses. Sporadic herpes virus was non-seasonal.⁷⁶ Among children with pharyngitis, adenovirus was recovered from 23%, herpes hominis virus from 8%, ECHO virus 3% and Coxsackie virus from 3%. *C. diphtheriae* was present in one, but *Mycoplasma*, rarely.⁷⁷

Respiratory syncytial viruses caused the most illness among infants and children, often severe and pneumonic. Parainfluenza viral illness was more prevalent and milder among outpatients. Pneumococci and *H. influenzae* present in 9% of children in hospitals also were isolated from ambulatory patients. Their relation to the illness often was uncertain.⁷⁸ In another study among children, respiroviruses caused 40% of infections, pneumococci 20%. In many children neither viruses nor bacteria could be associated with respiratory tract infection.⁷⁹ Pneumonia in young adults was caused chiefly by *M. pneumoniae* (54%) in late summer and autumn, and by adenoviruses (13%) in the spring.⁸⁰

Other viral infections

In a 2-week period, five children in a family contracted what presumably was varicella. Two were mildly sick and two of three with pneumonia died.⁸¹ Heroic measures were recommended for the treatment of varicellar pneumonia.⁸²

Herpes viruses

Diverse observations were made about herpes hominis viral infections. The virus seldom invades the respiratory tract of adults when specific antibody is present.⁸³ Pulmonic infection occurred in a transplanted lung probably caused by a resident virus activated as the result of immunosuppressive therapy.⁸⁴ Herpes viruses types 1 and 2 caused

genital infections in six children.⁸⁵ Herpes type 2 viral antibody was present in 83% of patients with uterine cervical carcinoma, but in 0–20% of control subjects. The finding suggested a carcinogenic or cocarcinogenic role of the virus,⁸⁶ but perhaps the virus was commensal or invasive in abnormal tissue. The virus caused three crops of vesicles in as many years in an anti-smallpox vaccination scar.⁸⁷ Herpes hominis infection associated with repeated attacks of neuralgia may be mistaken for that of herpes zoster.⁸⁸ Generalized infection and encephalitis caused by herpes virus were recognized oftener than in the past. Six instances were described.⁸⁹ The virus also is often present as a commensal.

Herpes virus inoculated intranasally⁹⁰ or subcutaneously⁹¹ in mice spread centripetally via the trigeminal or peripheral nerves to the central neural system confirming Goodpasture's view of 1925 and Johnson's in 1964. The viscera were not infected nor did viremia occur. Particles resembling those of the herpes virus group were in the spinal ganglion neurons of healthy guinea-pigs. If virus were present, it is so either as a commensal or a latent infection. Otitic herpes in man was described in 1907. Mumps, measles and the 'respiratory viruses' are causes of deafness.⁹²

Topically applied α -keto- β -ethoxybutyraldehyde hydrate (Kethoxal) had an active anti-herpes viral action in animals.⁹³ Interferon induced by a double-stranded RNA polymer promoted recovery from herpetic keratoconjunctivitis when applied 3 days after inoculation of rabbits.⁹⁴ DIQA (3,4-dihydro-1-isoquinoline acetamide hydrochloride) was active *in vivo* against a number of viruses, but inactive *in vitro*.⁹⁵

Enteroviruses

ECHO virus type 5 caused illness in fifty-six infants and eight adults during 16 weeks in Singapore with the usual wide range of clinical features, but without deaths or serious sequels.⁹⁶ ECHO virus 22 appeared to play a causal role in acute respiratory tract infections of sixty-four premature infants, seventeen of whom had pneumonia, one meningoencephalitis and another had hepatitis in addition.^{96a} Reports linking ECHO and Coxsackie viruses to hepatitis were cited.⁹⁷ ECHO virus 11, a relative of the rhinoviruses, invades both the respiratory and the enteric tracts. Infection was passed to volunteers by intranasal inoculation and by oral ingestion.⁹⁸ Virus type 11 caused febrile illness, occasionally encephalitic, in Canadian children.⁹⁹

Coxsackie virus type B2 caused an outbreak of acute respiratory tract infection in sixteen young children. Vomiting and diarrhea accompanied illness in nine.¹⁰⁰ In an epidemic in Finland, B5 virus caused eighteen cases of carditis or pericarditis or both, twenty-six cases of meningoencephalitis and ten of

pleurodynia.¹⁰¹ A10 virus caused 'hand-foot-and-mouth-disease' among children in New Zealand. Similar disease occurs with A5 and A16 virus infections. Antibody to A10 virus was detected in 50% of persons older than 5 years.¹⁰² Coxsackie A-like virus isolated from five patients may have caused epidemic lymphocytosis in twenty-seven children. The leukocyte counts ranged between 16,000 and 94,000 cells, at least 50% of which were lymphocytes.¹⁰³ ECHO 6, Coxsackie B and Reo viruses, as happens with *Salmonella* and mumps virus, were recovered from healthy dogs.¹⁰⁴ They may serve as sources of infection for man. A monograph summarized knowledge about Echoviruses and Reoviruses.¹⁰⁵

Viral hepatitis

The incidence of hepatitis 'peaked' in 1953 and 1961, and is rising again. The mortality is about 0.5% per 100,000 population. Mild and inapparent infections are far more common than statistics show.¹⁰⁶ A review was entitled 'Changing concepts in the epidemiology of viral hepatitis', but concepts have not changed much. Infectious hepatitis may be transmitted in blood, serum hepatitis may be spread by the fecal-oral route and a resulting chromosomal disturbance may have a bearing on mongolism. The cause still is unknown.¹⁰⁷ In a 9-week period, four nurses in a hospital contracted hepatitis. Survey of personnel with various screening methods failed to disclose 'subclinical' (etymologically sub or under, klinikos, the bed!) cases.¹⁰⁸ Because hepatitis may be transmitted in pooled plasma, once thought to be safe, albumin now is recommended instead for injection.¹⁰⁹ Post-transfusion hepatitis followed cardiac surgery in 53% of patients given blood from paid donors.¹¹⁰ One-unit transfusions of blood are unwarranted.

Acute pancreatitis occurred in four victims of infectious hepatitis. In others, the lymphatic, hematologic and renal systems also were involved.¹¹¹ Fine details of the lesions, but no viral particles were portrayed by electron microscopy.¹¹² Official recommendations for the use of immunoglobulin for preventing infectious hepatitis were published.¹¹³

Viral hepatitis in Ghana when associated with deficiency of 6-phosphate dehydrogenase had a long, severe course, as noted also during pregnancy.¹¹⁴ A self-limiting febrile disease with granulomatous hepatitis occurred in Israel. It resembled infectious mononucleosis and the cause was not found.¹¹⁵ Adenovirus was present in the feces of apes implicated as carriers of human hepatitis virus, but its relation to the disease is unknown.¹¹⁶ There is some evidence linking the 'Australia antigen' to hepatitis. It was present in the blood of 20-30% of patients, but in only 0.5% of normal persons.¹¹⁷

Infectious mononucleosis

Further studies on infectious mononucleosis confirmed previous reports of the appearance of complement-fixing antibody for the herpes-like virus (HLV) derived from a Burkitt-tumor cell-line. Other antibodies did not develop. Additional study is needed to establish the causal role of HLV in the disease.¹¹⁸ Although herpes-like particles occur and specific antibody appears, both were found with equal frequency in normal persons, in Burkitt's tumor and in leukemia. The serologic reaction may be another hetero-antibody response not indicative of a viral infection.¹¹⁹ Cultured circulating leukocytes from victims of infectious mononucleosis harbored virus-like particles resembling an RNA-incomplete tumor virus,¹²⁰ but no virus grew from circulating lymphocytes from a patient after month-long cultivation.¹²¹ Many persons who had antibody to EB virus associated with Burkitt lymphoma cells did not acquire mononucleosis, and all infections occurred among those without prior antibody. Some heterophile-negative patients also develop EB viral antibody and others with a mononucleosis-like disease do not. EB antibody is commonly found in normal persons, but overt mononucleosis is rare.¹²² There is no clinical evidence that infectious mononucleosis precedes or is related to any tumors. Further knowledge is needed before the virus can be said to cause the disease. Two infant sisters with mononucleosis died from hepatitis and hepatic failure. Leukemia was suspected in one.¹²³

Cytomegalovirus

Cytomegalovirus in eleven young adults was a mild disease characterized variously by respiratory tract involvement, gastro-enteritis, lymphadenopathy, conjunctivitis, exanthem, vaginitis, headache and anemia.¹²⁴ Ten per cent of healthy children less than 5 years of age, but only one adult excreted cytomegalovirus. Overtly infected children often have a protracted pertussis-like illness or hepatic injury. Twenty-five adults in a locality had mononucleosis-like disease, but in most other instances infection was inapparent.^{125, 126} Cytomegalovirus complement-fixing antibody occurred in 24-58% of healthy children and adults.¹²⁷ The virus was cultivated from circulating leukocytes of a leukemic patient.¹²⁸ Because of a high antibody titer in the serum of a patient, cytomegalovirus was thought to be the cause of nonicteric hepatitis and relative lymphocytosis.¹²⁹ The fluorescent macroglobulin test was a sensitive method to detect cytomegaloviral disease.¹³⁰

Myxovirus found in muscle may be a cause of polymyositis as a chronic viral infection,¹³¹ but virus-like particles also were present in the muscle but not elsewhere in a healthy man who died of

heat-stroke. The virus may have been commensal or represented latent infection.¹³²

Encephalomyocarditis virus infection in mice caused diabetes-like hyperglycemia by destroying β -cells in the islets of Langerhans. The pancreases contained large amounts of virus. Abnormal metabolism of glucose persisted after recovery from the infection.¹³³ Experiments in infected mice showed that continued administration of interferon was helpful and also may be of value in the treatment of other viral diseases.¹³⁴

The clinical course, pathological changes and virology in twenty-three patients infected by handling green monkeys were described in seven papers in the March 22 1968 issue of the *Deutsche Medizinische Wochenschrift*. In another report, the Marburg virus apparently was transmitted from person to person during coitus. Immunofluorescent technique revealed viral antigen in the sperms. Infection also is transmissible to guinea-pigs.¹³⁵ The causal agent contains RNA and appears to be a unique large virus.¹³⁶

An unusual pox-like, viral dermal infection was contracted from Asiatic monkeys.¹³⁷ In a colony of 1050 monkeys, 223 died during an epidemic of newly recognized viral hemorrhagic fever. No persons were infected.¹³⁸ Orf (ecthyma contagiosum), a self-limiting dermatosis acquired chiefly from sheep, affected nineteen persons in Kentucky and California. Viral particles containing DNA like those of the poxvirus group were visualized by electron microscopy.¹³⁹

Virus-tumor relationship

Studies as usual pertained chiefly to animals. Lymphoma appeared in a rabbit 7 months after the inoculation of a reovirus originally isolated from Burkitt's lymphoma.¹⁴⁰ Other viruses also have been found in Burkitt's tumor. Oncogenic viruses induced malignant change of 50% of animal cells when grown together *in vitro*.¹⁴¹ After special treatment, adenoviral tumor cells served as an immunizing antigen against tumors caused by the same cells in hamsters.¹⁴² Yaba tumors are histiocytomas in African monkeys caused by a member of the poxvirus group. It caused similar growths in inoculated volunteers. Tumors regress within a month or two.¹⁴³ Virus-like particles in blood from patients with neoplasms of the blood-forming areas were no different from those found in healthy persons.¹⁴⁴ Antibody present in the blood of patients with osteosarcoma and of persons in close contact with them suggested an association with an infectious agent which causes unrecognized infections in the healthy persons. The agent may be an 'incidental passenger'.¹⁴⁵

Antiviral vaccines

The successful use of live rubella virus vaccine was reported in four papers in the June 1968, *American Journal of Diseases of Children*, and in others elsewhere. Antibody in vaccinees persisted for a year¹⁴⁶ and infection did not spread to others.¹⁴⁷ Injected γ -globulin suppressed the development of overt rubella, but failed to reduce the incidence of infection in susceptible pregnant women. Twenty-six of forty-one with serologic evidence of infection had asymptomatic disease.¹⁴⁸

Inactivated mumps virus vaccine reduced the incidence of mumps by 94% among Finnish soldiers. The incidence of orchitis was lower among the vaccinees.¹⁴⁹ Vaccination was 95% effective among 3000 school children. No untoward reactions were observed.¹⁵⁰ Mumps vaccine should not be given to persons sensitive to egg-protein or neomycin, nor to victims of neoplastic diseases or during pregnancy.¹⁵¹

Immunization with live attenuated measles vaccine without immunoglobulin was followed by fever in 25% of children and a rash in 51%. Respiratory tract involvement also occurred.¹⁵² After a state-wide vaccination campaign, only forty-nine cases of measles were discovered, suggesting that the disease is nearly 'eradicated'.¹⁵³ One wonders if it ever will be.

Pertussis immunization did not give lasting protection. In one study, attack-rates ranged from 20 to 50% of vaccinees. After 12 years, the rate was 95%. In adults, pertussis often was mild without any whooping.¹⁵⁴ A vaccine administered orally is under investigation for the prevention of shigellosis.¹⁵⁵

A council recommended procedures of immunization against a variety of infections.¹⁵⁶ At present, about twenty-six vaccines and antitoxins are available, and more are under study. Progress in the control of viral diseases with vaccines, chemicals and interferon was summarized.¹⁵⁷

Reactions to vaccines

Among forty-one children vaccinated in 1961-62 with killed and live measles vaccines and reimmunized with live vaccine in 1965, eighteen had untoward reactions which were severe in four.¹⁵⁸ Inoculation of live measles vaccine with γ -globulin probably caused fatal, sclerosing panencephalitis 3 weeks afterwards.¹⁵⁹ Fatal epidermal necrolysis and pneumonia followed 3 hr after the injection of measles vaccine in an infant.¹⁶⁰ Tuberculous meningitis with drug-resistant bacilli after measles vaccination ended fatally in a child.¹⁶¹

Malignant tumors arose in anti-smallpox vaccination scars in twenty-five patients.¹⁶² In two instances, tumors appeared at bilateral sites. It was uncertain if coincidence or causal relation was involved. Convulsive reactions followed vaccination at the rate of 1.5/1000 among infants and young children. One

in 4000 resulted in cerebral injury.¹⁶³ Because about 240 deaths from the complications of anti-smallpox vaccination have occurred since the last fatal case of smallpox in the United States in 1948, and because smallpox is less contagious than other viroses, Kempe continued to question the need for routine vaccination. Other safer methods were described.¹⁶⁴ Avian leukosis virus if present in yellow fever vaccine can be removed by differential filtration.¹⁶⁵

γ -Globulin

γ -Globulin often is used without reason. It is useful for persons when vaccination is contraindicated or if vaccine is unavailable. γ -Globulin may prevent rubeola but only when injected soon after exposure. It may merely mask rubella. It may modify viral hepatitis, but does not prevent infection. It is not indicated for varicella and its use for other host-globulin defects is uncertain.¹⁶⁶ Viral respiratory tract infections are uninfluenced. Adverse reactions were described.¹⁶⁷

Interferon

Progress in studies of interferon was summarized.^{168, 168a} Besides viruses, interferon is induced by bacteria, rickettsiae, protozoa, toxins, synthetic polymers, pentnucleotides and other non-viable agents. Interferons are a general, nonspecific, broad-spectrum defense system of hosts. They are elaborated after contact with substances that have neither biologic nor chemical relation to the agent against which they protect. They may eventually be applied therapeutically, but there is little hope for using exogenous interferon for prophylaxis or treatment. By some means, it should be induced in the infected person, but adverse and beneficial effects may follow. Studies are in progress to see if the intravenous injection of synthetic viral nucleic acid will displace a naturally present intracellular virus.¹⁶⁹ An antiviral drug, Aranotin, having 100 numerals and letters in its chemical name, was proposed for clinical trial.¹⁷⁰

Bacillary infections

Salmonella was the leading cause of 'food poisoning' in the United States. In 1967, thirty-five outbreaks accounted for nearly 13,000 victims. Beef and turkey meat, eggs and milk were the chief sources. *Clostridia* accounted for twenty-nine outbreaks and 3500 cases.¹⁷¹ Many more unreported infections no doubt occur. No significant change in the incidence of antimicrobial-resistant salmonellas was noted in the past five years. Of fifty-two strains resistant to several drugs, forty-one had the resistance-transfer factor.¹⁷² Antimicrobial drugs had no effect in shortening the course of salmonellar dysentery. They may prolong the excretion of the bacilli.¹⁷³

Forty-nine of 232 strains of *E. coli* from hospital patients had the resistance-transfer factor.¹⁷⁴ A 3-month epidemic of dysentery in adults presumably was spread by water-borne *E. coli* 0111: 34.¹⁷⁵

Brucella suis infection contracted from a deer caused chronic, indolent dermal ulcers in a previously lacerated area.¹⁷⁶ Pancytopenia occurred in a patient with brucellosis.¹⁷⁷ *B. abortus* grew in cultures of nineteen samples of insufficiently heated cream and cream products.¹⁷⁸

In a Calcutta slum, stools from nine members of five families, none of whom had been exposed to cholera, contained *V. comma*.^{178a} Evidently, and contrary to an old idea, healthy carriers are not rare. In the absence of vomiting, the need for intravenous injection can be reduced by the oral ingestion of a solution of glucose, sodium chloride and potassium chloride.¹⁷⁹ By electron microscopy, cholera vibrios unlike *Shigella*, did not penetrate the enteric epithelium which remained intact.¹⁸⁰

Pseudomonas caused infection of cartilaginous areas in puncture wounds of the foot in eleven children in spite of large doses of many antimicrobial drugs. Surgical debridement was needed, but residual skeletal damage ensued.¹⁸¹ The exotoxin of *Pseudomonas* when injected into dogs caused an anaphylactoid reaction. Pre-treatment with immune serum prevented death, but had no effect on the allergic reaction.¹⁸²

Labile blood-pressure, vasoconstriction, diaphoresis, fever, hypotension and increased catecholamine output are indications of an over-active sympathetic nervous system in tetanus.¹⁸³ Fatal gas-gangrene followed intramuscular injections of epinephrin¹⁸⁴ as had been reported previously by others.

The first outbreak of tularemia in Switzerland was observed among butchers who handled rabbit-meat.¹⁸⁵ Therapy with streptomycin and tetracycline or chloramphenicol cured fifty-eight Vietnamese patients with plague.¹⁸⁶ Between 1900 and 1966, 547 plague cases were reported in the United States, mostly west of the 97th meridian, where wild-rodent carriers live.¹⁸⁷ Unrecognized cases, no doubt, occur. Melioidosis apparently was acquired in a laboratory presumably by inhalation.¹⁸⁸

Serratia marcescens became important as a nosocomial invader when resistance of the body was impaired iatrogenically.¹⁸⁹ In one hospital, contaminated nebulizers probably were the source of infection of thirty-eight patients, eighteen of whom died.¹⁹⁰ In a diabetic patient, the bacillus caused arthritis which resisted therapy and amputation was required.

Typhoid

The clinical behavior of typhoid was said to be changing. In India the onset in eighty-two of ninety-

eight cases was insidious, bronchitis occurred in 50% and encephalopathy in 44%. Rose spots and relative bradycardia were rare, but intestinal perforation occurred in three, of whom two died, and two had bleeding. Probably because of longer survival after antimicrobial therapy, the incidence of circulatory failure and encephalopathy was commoner than before. Six patients in Nigeria responded as well to treatment with trimethoprim and sulfamethoxazole as with chloramphenicol.¹⁹³

Serologic tests for typhoid often are nonspecific and difficult to interpret. The titer for O antigen is most meaningful. Test for Vi agglutinin is of little value to detect carriers.¹⁹⁴ Vaccination failed to protect six Peace Corps persons from typhoid in India during a 2-year period.¹⁹⁵

Tuberculosis

Depending upon the region of the United States where tests are made, a second antigen (PPD-B) against atypical mycobacteria applied in addition to the standard PPD test, served to differentiate genuine tuberculosis from other forms. In different regions, 12–30% of persons reactive to the standard test did not have tuberculosis.¹⁹⁶ Cervical adenitis caused by atypical mycobacteria was considered to be an entity different from that caused by *M. tuberculosis*. Surgical excision of the involved lymph nodes was advised.¹⁹⁷ Fatal disseminated infection with atypical mycobacteria was associated with pancytopenia in three patients.¹⁹⁸ Group IV bacilli caused endocarditis.¹⁹⁹ Bacilli present in sarcoid-like tissue of several patients may have been commensals or causes of co-existing infection or one cause of sarcoidosis.²⁰⁰ Mycobacterial dermal ulcers containing great numbers of acid-fast bacilli commonly occur in the Nile river region. The infection was first observed in Australia.²⁰¹

Ethambutol and capreomycin were used in combination with isoniazid. Although most of 277 patients were infected with isoniazid-resistant bacilli, 75% were freed of the bacilli.²⁰²

Progress in the field of leprosy lags. The bacillus has not yet been cultivated *in vitro*, BCG vaccination failed in Burma, and the bacillus may become resistant to the drugs in current use.²⁰³ There are 2500 lepers in the United States and an estimated 10 million in the world.²⁰⁴

Coccal infections

Staphylococcal infection

During the early period of a 10-year study in a hospital, neither strict prophylactic nor antimicrobial therapy overcame the virulence and spread of type 80/81 staphylococci. Some unknown influence

accounted for their disappearance by 1965 and a resulting decrease in nosocomial infections. Staphylococcal epidemics, like others, recur cyclically.²⁰⁵ In another hospital, three kinds of staphylococci existed: penicillin-sensitive, moderately penicillin-resistant and highly resistant ones. The latter spread within the hospital. Penicillin therapy and also the use of chloramphenicol, tetracycline, kanamycin and erythromycin brought about moderate to high penicillin-resistance.²⁰⁶ Methicillin-resistant staphylococci have increased in incidence especially as causes of nosocomial infections. Only 40% of sixty-six strains were inhibited by other antimicrobics, but all were sensitive to vancomycin.²⁰⁷ Resistant strains were not detected in a Boston hospital until 1967 where after a year they were isolated from eighteen patients.²⁰⁸ In Germany, methicillin-resistant strains increased from 10% in 1965 to 16% in 1967.²⁰⁹

In a Seattle hospital, the incidence of antimicrobial-sensitive strains increased over a 9-year period. Staphylococcal bacteremia declined in patients probably because of controlled conservative therapy, by minimizing inappropriate therapy and for other reasons.²¹⁰

Among forty-four instances of hospital-acquired infection, venous catheters in place for more than 48 hr were responsible for nineteen. *S. aureus* was causal in thirteen, bacilli in five and a yeast in one. After the tube was removed, seventeen patients recovered without antimicrobial therapy.²¹¹ Bacteremia in 185 patients affected chiefly the very young, the very old, patients with chronic disease and post-operative wounds, and after intravenous catheterization and dermal trauma. The mortality rate was 42%, and for *S. albus* 28%. The mortality rate before 1940 was 82%. At that time, only 29% of patients had underlying illness as compared with 75% after 1952.²¹²

A patient who died at age 19 years, had had chronic granulomatous disease since infancy, caused by staphylococci, which his neutrophil cells failed to kill, and his blood lacked specific antibody. Immunization with toxoid gave temporary improvement.²¹³ In another study, three sibling children, who were immunologically competent, had chronic granulomatous disease with staphylococcal abscesses and bacteremia. Their neutrophils also were unable to kill the cocci *in vitro*.²¹⁴

Streptococcal infections

Despite modern management, hemolytic streptococci caused puerperal fever in twenty women during 5 days in a hospital in 1965, the first epidemic there in 33 years. All patients recovered after penicillin therapy.²¹⁵ In another hospital, nine women were infected apparently from colonized umbilical stumps of their infants.²¹⁶

Ninety-five cases of streptococcal pneumonia affected naval personnel during 19 months without antecedent viral respiratory tract infection. Empyema occurred in fifty-four.²¹⁷ Three outbreaks of acute nephritis in Trinidad since 1952 probably were of streptococcal origin.²¹⁸ The skin as well as the throat may serve as a source of renal involvement.²¹⁹ Cocci of Group A, type 12 present in a patient and in four persons in his vicinity resisted tetracycline, erythromycin and lincomycin.²²⁰

In spite of the recommended oral dosage of penicillin, hemolytic streptococci persisted in the pharynx of 10–25% of children with acute streptococcal pharyngitis. The relapse rate was higher when M-typable strains were invasive, especially types 3 and 12.²²¹ For the prophylaxis of recurrent rheumatic fever, the streptococcal infection attack-rate in persons receiving parenteral injections of penicillin was 6.6/100 patient-years and a rheumatic recurrence-rate of 0.6%. For those given penicillin orally, the respective figures were 22.7 and 4.8%.²²² Sulfamethoxazole was said to be as effective as penicillin for curing streptococcal pharyngitis,²²³ but according to general opinion sulfonamides do not eradicate streptococci.

The persistence of Group A streptococcal antibody is peculiar to rheumatic valvular disease, but its pathogenic significance is unknown.²²⁴ In South Africa, 8% of 300 sections of renal biopsies had characteristics of 'analgesic' nephritis, not of streptococcal infection.²²⁵

Non-hemolytic streptococci appeared in the blood within 5 min after exodontia in eleven of 100 children, but in only four who received penicillin beforehand. The cocci often resisted one or more antimicrobial drugs.²²⁶

Endocarditis

Vancomycin was effective in the treatment of endocarditis due to penicillin-resistant non-hemolytic streptococci or if the patients were sensitive to penicillin.²²⁷

Endocarditis caused by coagulase-negative staphylococci occurred in 10% of patients in a hospital. Few of the cocci resisted penicillin. Nine of twenty-three patients died. The overall cure-rate was 60%.²²⁸ Endocarditis caused chiefly by staphylococci, streptococci and candida affected forty-one narcotic addicts.²²⁹ It accounted for 8% of deaths of addicts. Diphtheroid bacilli caused endocarditis in two patients after the insertion of a prosthetic valve.²³⁰ Protoplasts were present in an aortic valve during enterococcal infection. Valvectomy was curative.²³¹

Gonorrhea

Among 118 pregnant women, thirty-seven had complicating gonorrhea and of these, less than half

delivered viable infants. About 6% of prenatal-clinic patients carried gonococci.²³² Gonococcal arthritis still occurs especially in women.²³³ A 2-g dose of kanamycin cured 93% of 155 patients with urethritis.²³⁴

Meningo-encephalitis

The first recognized epidemic of St Louis encephalitis in the Philadelphia area occurred during a drought in early fall, 1964. Nearly 120 cases were recorded and 11 elderly patients died.^{234a} No doubt, many mild, inapparent and undiagnosed infections also occurred. California virus caused encephalitis in thirty-five children during summer months in Wisconsin. Residual impairment persisted for 6 years in seventeen.²³⁵

An encephalitogenic agent from the brains of patients with subacute sclerosing panencephalitis when transmitted to ferrets caused ataxia 5 months later. Further transfer shortened the incubation time.²³⁶ Measles antigen and syncytial formation were described in cultivated cells from a patient's brain.²³⁷ Spongiform encephalopathy (Creutzfeldt-Jakob disease), a chronic malady, was transmitted to chimpanzees by inoculating cerebral tissue from a patient. The lesions after 13 months resembled those of kuru. A transmissible agent presumably was causal.²³⁸

Sixteen deaths from amebic meningo-encephalitis occurred in Czechoslovakia. Infection presumably was acquired in an indoor swimming-pool.²³⁹ In Virginia, amebas were present in two of 390 samples of spinal fluid, *Naegleria* in a fatal case and *Acanthameba* in one with recovery, the first of such reported. Antimicrobial therapy failed.²⁴⁰ It is of importance to test swimming-pool water for the presence of amebas. Many cysts resist chlorination.²⁴¹

E. coli caused meningitis in three adults, two of whom died.²⁴² In a non-epidemic period, from 3 to 8% of members of families carried meningococci group B in the nasopharynx. Twenty-eight per cent resisted at least 0.1 mg/100 ml of a sulfonamide drug.²⁴³ Group B hemolytic streptococci caused meningitis in two patients who had other underlying disease.²⁴⁴

Pneumonias

H. influenzae may cause lobar or segmental pneumonia in persons whose lungs were injured previously, and diffuse, miliary, occasionally afebrile broncho-pneumonia in old persons with chronic pulmonic disease. Cigarette smoking is a contributing causal factor. Ampicillin or tetracycline is the drug of choice for treatment.²⁴⁵ A previously healthy adult had pneumonia caused by *Pseudomonas*. Penicillin G, tetracycline, mycostatin, procaine penicillin, colistimethate, chloramphenicol, erythromycin, strepto-

mycin, polymyxin, gentamicin and prednisone were given in succession. Death followed after 6 months of 'haphazard administration' of drugs.²⁴⁶ Pneumatoceles appeared in four patients after staphylococcal pneumonia.²⁴⁷ I described these characteristic sequels in 1933.²⁴⁸ Pneumonias caused by *Mima*²⁴⁹ and by ascaris²⁵⁰ were described. Mycoplasmal and adenoviral pneumonia were complicated by acute renal failure from the cold-agglutination syndrome.²⁵¹ It is unusual for adenovirus to incite cold-agglutination. Tetracycline given prophylactically to naval recruits did not prevent pneumonias, but seemed to shorten the course.²⁵²

Urinary tract infections

Active progressive chronic pyelonephritis occurred without evidence of bacterial cause. Prior infection may have been present.²⁵³ Possible viral infection was not mentioned. Mice inoculated with ECHO 9 virus developed acute glomerulonephritis which healed after 6 weeks. Viral antigen persisted for 54 days. The virus was either the direct cause or an antigen-antibody reaction was involved.²⁵⁴ In the November 1968 issue of this journal, I reviewed the relation of viroses to renal infection. The kidneys often are involved, but seem to be more resistant to injury than other organs and tissues. They rarely bear the brunt of infection. Evidence of viral nephritis or nephrosis seldom is of serious import and may be indistinguishable clinically from that of other cause.²⁵⁵

Human urine often is bacteriostatic or bactericidal for small numbers of colon bacilli, especially when the amount of urea is high.²⁵⁶ Rendering the urine alkaline (pH 6.0-8.2) greatly enhanced the activity of erythromycin against Gram-negative bacilli and some Gram-positive cocci.²⁵⁷ Continuous therapy with methenamine mandelate, nitrofurantoin or sulfamethizol was ineffective in inducing a favorable bacteriologic response unless initial therapy had greatly suppressed or eradicated bacteriuria. The response-rate was lowest after multiple prior courses of therapy had been applied.²⁵⁸ Antibody to serogroups of *E. coli* was higher than in control patients, but no bacilli were recovered in one-third of them. Demonstration of the antibody may aid in diagnosis and therapy.²⁵⁹

Mycoses

Cryptococcus neoformans was present in the sputum of seventeen patients with pulmonic disease, but its invasiveness was doubtful. None was treated with amphotericin B and the yeast disappeared in all but one. Other disease accounted for the illnesses. The yeast usually is commensal. *H. capsulatum* was present similarly in eighteen patients, and *B. dermatitidis* in twelve.²⁶⁰ In another study, *C. neoformans*

was isolated from the sputum or lungs of thirty-two patients, and was invasive in eight and probably so in six. Unless diagnosis is positive, therapy with amphotericin B is best withheld.²⁶¹ Sixteen instances of proved or presumed histoplasmal pericarditis are on record.²⁶²

Exotic infections

Attention was called to the importance of malaria, amebiasis, trypanosomiasis, leishmaniasis and helminthic diseases in New York City and in other metropolitan centers. It becomes more and more necessary to know where patients had been (*unde venis?*) and to suspect diseases that are endemic abroad but exotic here.²⁶³ The possibility of the diseases mentioned and, in addition, plague, melioidosis and shigellosis must be considered in returnees from south-east Asia.²⁶⁴ Infected military personnel returning from Asia have increased the incidence of lymphogranuloma venereum in the United States.²⁶⁵ Methods to detect imported exotic infections were outlined.²⁶⁶

Malaria. Five patients with cerebral falciparum malaria died from acute pulmonary edema. Whether the pulmonary microcirculation was obstructed²⁶⁷ or a central influence was causal is unknown. A therapeutic combination of sulfalene and trimethoprim controls some falciparum infections resistant to other drugs. A prophylactic drug is needed.²⁶⁸ Primaquine injured plasmodia in the exoerythrocytic state. Electron microscopy showed swollen mitochondria and cytoplasmic vacuoles.²⁶⁹ After feeding on infected monkeys, mosquitoes bearing *P. falciparum* transmitted the disease to volunteers.²⁷⁰ An indirect hemagglutination test gave positive results in 98% of cases of malaria and in less than 1% of uninfected persons.²⁷¹

Amebiasis is endemic among Amerinds in Saskatchewan, and dysentery with hepatic abscess is not uncommon as discussed in four papers in the 12 October issue of the *Canadian Medical Association Journal*. The capillary-tube precipitin test provided a simple rapid method to detect amebic dysentery and hepatic abscess.²⁷² Infectious diseases endemic in circumpolar areas were discussed in a symposium in the October issue of the *Archives of Environmental Health*.

Pinta was transmitted experimentally to chimpanzees.²⁷³ Kuru-like symptoms appeared after 23 months in spider monkeys inoculated with tissue from patients.²⁷⁴ A dinoflagellate responsible for the 'red tide' in the North Sea in May and September caused death of marine life and seventy-nine poisonings of persons who ate mussels, as described in four papers in *Nature* of October 5.

The second case of infection with a piroplasma of the genus *Babesia* was reported. The disease is

common among animals in Africa. It was mistaken for malaria in a patient in California. Splenectomy was done and recovery followed therapy with chloroquine.²⁷⁵ Cycloguanil pamoate (Camolar) was successful in the treatment of most cases of cutaneous leishmaniasis.²⁷⁶

Immunity problems

Reviewing the immunologic response to infection, Cluff points out that microbic infections may induce immunity or harmful effects or no effect. The problem is complex and varies greatly according to the causal microbe, to delayed reactions and to autoimmunity. The Wassermann reaction, the rheumatoid factor, amyloidosis and other sequels are involved.²⁷⁷ Progress in immunology dealing with syndromes of diminished resistance to infection also was reviewed.²⁷⁸

Rhythmic changes in the function of neutrophil cells and also corticosteroid therapy contribute to immunosuppression. The neutrophil action on bacteria fluctuated in cycles of 15–21 days in men and 24–32 days in women²⁷⁹ calling to mind the frequency of infection during the neutropenic phases in episodes of periodic myelodysplasia (neutropenia).²⁸⁰ Familial phagocytic-plasmal defect besides hypogammaglobulinemia was said to favor infection²⁸¹ as discussed in the section on staphylococcal disease. Mycotic infections chiefly with *C. albicans* occurred in twelve patients with lupus erythematosus treated with steroids. Death followed in eight.²⁸²

Pneumocystis carinii was recovered at necropsy from five patients with lymphoma as compared with 0% of patients with other diseases.²⁸³ Exposure to new antigens elicits poor antibody responses in lepers²⁸⁴ and in diabetic patients as Moen and I showed 36 years ago.²⁸⁵

Infections after hepatic homografts are similar to, but more fulminating than those after renal transplantation. Of seventeen patients, many developed bacteremia, mycotemia or cytomegaloviral infection and died after 4–6 months. With improved technique, four patients were free of serious infections for 2–5 months.²⁸⁶ The risk of bacteremia from intravenously inserted polyethylene catheters was 2%. Phlebitis occurred in nearly 40% of instances. The risk is in proportion to the duration of use.²⁸⁷ After cardiac surgery in sixteen patients, serologic evidence of cytomegalovirus appeared in seven and the virus was in the urine or throat or both in three. It may have been inoculated in transfused blood.²⁸⁸

Miscellaneous items

Q fever

In an endemic area of Q fever in Texas, eight of fifty-two cases of pneumonia were caused by *Coxiella burnetii* which presumably was airborne.

The clinical course was identical to that of viral pneumonia. Tetracycline was effective therapeutically.²⁸⁹ Curiously, pulmonic involvement rarely occurred among sixty-seven infected abattoir workers in Australia. Instead, prolonged fever, hepatitis and endocarditis were serious features.²⁹⁰ Twenty-three cases were observed in northern Ireland.²⁹¹ Two laboratory workers acquired typhus and two got scrub-typhus. The mode of infection was unknown in three. Abnormal hepatic function occurred in three.²⁹²

Rocky Mountain spotted fever affected thirteen persons in Massachusetts. Two died because of tardy diagnosis and delayed therapy.²⁹³ Reports continue to appear about thrombocytopenia, petechiae and purpura during acute infectious diseases as if the observations were new. The occurrences were first described as common to infections in general by Hayem 86 years ago. Thrombocytopenia was detected during Rocky Mountain spotted fever and regarded as a complication rather than as integral to the disease.²⁹⁴ It was noted in typhus by Helber in 1904.

Ornithosis in sixteen children was acquired from ducks, doves, parakeets and sparrows.²⁹⁵ Bedsonia as chlamydia are closely related to bacteria, not to viruses. Although they pass through filters, they contain both DNA and RNA, divide by fission, have a cell-wall and are susceptible to antimicrobics.²⁹⁶

T-strain *Mycoplasma* in the genital tract may be a cause of repeated abortion. In two instances, antimicrobial therapy was followed by normal parturition. Several instances of sepsis caused by *M. hominis* during pregnancy resulted in abortion.²⁹⁷ *Mycoplasma arginini* is a new species isolated from tissues of animals and of man. Its pathogenicity is undetermined.²⁹⁸ The double diffusion gel precipitation (ID) technique is a rapid, easy method to detect an antibody response for the diagnosis of mycoplasmosis.²⁹⁹

Toxoplasmic antibody, presumably after infection, occurred in three of 189 members of thirty-seven families, or 1/1831 person-months for those less than 20 years of age. Infection may be acquired from undercooked meat.³⁰⁰ Knowledge of toxoplasmosis was summarized in the 19 and 26 December issues of the *New England Journal of Medicine*.

It seems feasible to make diagnoses of toxoplasmosis, malaria, syphilis, rubella and cytomegalosis rapidly by means of an automated fluorescent technique.³⁰¹ Mechanical identification of bacteria by means of electronics and fluorescein-labelled antibody was said to approach the accuracy of current routine diagnostic procedures, especially for group A streptococcal infection.³⁰² Another quick method for bacterial identification may be the demonstration of a specific 'light-scattering' effect brought about by monochromatic laser light.³⁰³

According to Gsell, the eradication of many infectious diseases will be possible in the near future.³⁰⁴ I am less optimistic and have expressed editorially a dimmer view of eradication unless a variety of obstructions can be overcome.³⁰⁵ Malaria is a case in point.³⁰⁶

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