Hospital-associated Viral Infection and the Anesthesiologist

G. C. du Moulin, M.S., M.P.H.,* and J. Hedley-Whyte, M.D.†

TRANSMISSION OF VIRUSES is a common event in hospitals.1,2 Severity of infection can range from the isolated subclinical infection of a single patient to full-blown epidemics involving large segments of the hospital. Most known viruses have been implicated in nosocomial infections, including some of exotic origin.3 Nosocomial infection resulting from viruses is probably responsible for more patient morbidity than nosocomial infection caused by bacteria, although substantiation of the true rate of nosocomial viral infection is incomplete. Infected anesthesia staff who have occupationally close contact to the mucous membranes of patients can serve as important links in the transmission of viruses between patients. By compromising immune defenses, anesthesia and surgery may worsen the course of viral illness.

Nosocomial viral infections can be differentiated from bacterial infection by three main criteria.1 First, nosocomial viral infections often reflect the prevalence of the virus in the community. These viruses are introduced into hospitals by patients and staff. Secondly, in contrast to bacterial infection, viral infections of the respiratory tract generally do not occur primarily in high-risk debilitated patients but in any patient. Finally, while much bacterial pneumonia is acquired from a patient’s endogenous flora, for example, by the aspiration of gastric bacteria,4 viral infections generally are acquired exogenously from staff and patients.

The extent of nosocomial viral infection is only just being learned. Hospital-acquired viral illness was estimated in 1978 by the Centers for Disease Control at 5,800 cases annually.2 A recent and more complete analysis carried out at the University of Rochester determined that 5% of nosocomial infections at their institution are of viral origin.2 Extrapolated nationwide, this translates into 75,000 infections annually. Even this figure is probably conservative because of a lack of definitive evidence of viral infection. Most hospitals still lack the diagnostic tools to identify specific viral infections. The more traditional collection of acute and convalescent sera is often not done unless there exists a specific interest to study a particular virus. The Rochester study revealed that 75% of nosocomial viral infections involve the respiratory tract. Infections acquired were caused by respiratory syncytial virus, parainfluenza virus, adenovirus, rotavirus, influenza virus, and rhinovirus.

In another study, 52% of patients admitted to a pediatric service acquired some form of viral illness during hospitalization, including rhinovirus, respiratory syncytial virus, parainfluenza, and influenza A and B.5 In only 3% of the cases was virus spread from a roommate. Medical personnel and visitors were found to be most responsible for shedding virus. One direct by-product of viral infection is increased bacterial infection, particularly pneumonia.6 In a study of 89 house officers who acquired a total of 82 viral respiratory tract infections during an 11-month period, airway colonization by Staphylococcus aureus present in 5–15% during illness-free periods increased to 43% during viral illness. Airway colonization with gram-negative bacilli increased from 12–18% to 60% when the house officers became

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ill. Virus infection of the respiratory tract predisposes to bacterial overgrowth with subsequent increase in morbidity.

We shall present the current state of knowledge of viral infections germane to the management and protection of the hospitalized patient and anesthesiologist. Consequently, we shall discuss hepatitis B virus, herpesvirus including varicella, respiratory syncytial virus, adenovirus, influenza/parainfluenza, rhinovirus, rubella, and Creutzfeldt-Jakob disease. A simplified classification scheme reviewing characteristics of these viruses is presented in table 1.

### Table 1. General Characteristics of Viruses Important in Hospital Infections

<table>
<thead>
<tr>
<th>Virus</th>
<th>Family</th>
<th>Genome</th>
<th>Diameter of Virus (nm)</th>
<th>Enveloped</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B</td>
<td>?</td>
<td>DNA</td>
<td>44</td>
<td>+</td>
</tr>
<tr>
<td>Herpesvirus</td>
<td>Herpesviridae</td>
<td>DNA</td>
<td>100–200</td>
<td>+</td>
</tr>
<tr>
<td>Varicella</td>
<td>Herpesviridae</td>
<td>DNA</td>
<td>100–200</td>
<td>+</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>Adenoviridae</td>
<td>DNA</td>
<td>70–90</td>
<td>+</td>
</tr>
<tr>
<td>Influenza virus</td>
<td>Orthomyxoviridae</td>
<td>RNA</td>
<td>80–120</td>
<td>+</td>
</tr>
<tr>
<td>Respiratory syncytial</td>
<td>Paramyxoviridae</td>
<td>RNA</td>
<td>150–500</td>
<td>+</td>
</tr>
<tr>
<td>Parainfluenza</td>
<td>Paramyxoviridae</td>
<td>RNA</td>
<td>150–250</td>
<td>+</td>
</tr>
<tr>
<td>Rubella</td>
<td>Toroviridae</td>
<td>RNA</td>
<td>50–75</td>
<td>+</td>
</tr>
<tr>
<td>Rhinovirus</td>
<td>Picornaviridae</td>
<td>RNA</td>
<td>20–30</td>
<td>+</td>
</tr>
<tr>
<td>Creutzfeldt-Jakob</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

* + = yes, * = no.

Hepatitis

Viral hepatitis is subdivided into three forms: hepatitis A—epidemic or short-term incubation period hepatitis; hepatitis B—homologous serum or posttransfusion hepatitis; and a third form for which the term "hepatitis C" or "non-A/non-B hepatitis" has been proposed.7 Hepatitis A virus is an infrequent cause of nosocomial infection. Anesthesiologists have never been implicated in transmission of this virus and are not at increased risk of hepatitis A infection. Hepatitis B, by contrast, is a common occupational hazard of anesthesiologists and other health care professionals,6–18 and they may be responsible for transmission of hepatitis B virus to patients.12,19

The anesthesiologist should note that there are five nonparenteral routes of transmission of hepatitis B, as well as the parenteral route.6,20–24 The nonparenteral routes are primarily, and most commonly, direct percutaneous inoculation by needle of contaminated serum or plasma or transfusion of infective blood or blood products. Less commonly, non-needle percutaneous transfer of infective serum or plasma can occur. The third most common route is introduction of infective serum or plasma onto mucosal surfaces. Introduction of infective secretions other than serum or plasma onto mucosal surfaces can give rise to transmission, as can indirect transfer of infective serum or plasma via vectors or inanimate environmental surfaces. Airborne transmission still is the subject of controversy.20,25

The anesthesiologist needs to be concerned with self-inoculation, as well as with patient inoculation. Infected staff unknowingly can transmit hepatitis B surface antigen to patients. This is especially important in light of the fact that one can be an asymptomatic carrier of hepatitis B surface antigen.5,10,15,29,26–30 The carrier state is defined as persistence of hepatitis B surface antigen for more than 6 months, and this state may be lifelong. The incidence rate of such carriers varies in different populations with a range of 0.1–20%.20 It has been reported that 5–50% of persons infected with hepatitis B virus become chronic carriers.27,30,31 The carrier's blood, and possibly other body fluids, maintain the infectivity for hepatitis B virus. The ability of hepatitis B virus to contaminate the environment further emphasizes the necessity for concern by anesthesiologists.32

Hepatitis B is a disease that has been shown to be transmitted by oral surgeons to patients.33,34 An oral surgeon who was an asymptomatic carrier of hepatitis B surface antigen infected 71 patients, although no hepatitis B surface antigen was found in the dentist's secretions and there were no overt breaks in aseptic technique. The oral surgeon had not worn gloves, and he admitted to finger cuts while working in the oral cavity.34 After having taken 7 months convalescence for hepatitis infection, an oral surgeon was still able to transmit the disease to his patient.35

Many analogies can be drawn between anesthesiologists and oral surgeons; however, there have been no studies examining hepatitis transmission in the practice of anesthesiology. One can only conclude that the anesthesiologist should make every effort to prevent the acquisition of hepatitis B. In the reverse situation during a recent outbreak of hepatitis B, an anesthesiologist was infected during operation on a bisexual drug addict who had been admitted to the hospital in an unconscious state. The surgeon, the operating room supervisor, and his intensive care unit nurse also contracted hepatitis B.35

A limited number of studies have looked at the exposure of physicians to hepatitis B virus.8,18 In one study, a total of 1,192 physicians at three consecutive annual meetings of the American Medical Association (AMA) were tested for the presence of hepatitis B surface antibody, an indicator of prior exposure.9 Overall, 18.5% of physicians showed evidence of exposure. Surgeons had the highest frequency with 28% and anesthesiologists had 17%. These figures should be compared with
A 4% positive exposure rate in physicians involved in nonpatient care activities. In a recent study from Germany, both hepatitis B surface antigen and hepatitis B surface antibody were measured in a population of 3,770 hospital personnel. Physicians as a group had a frequency of exposure of 18%, similar to that obtained in the AMA study. However, when exposure rates to hepatitis were examined by departments, those of dialysis and anesthesia were highest at 31%. The rate of German anesthesiologists may be double the AMA meeting attendees' rate because the Germans anesthetize twice as many patients per year as anesthesiologists who attend the American Medical Association meeting. One-quarter of German surgeons exhibited evidence of exposure to either antigen or antibody. Personnel from non-patient-care disciplines had a 7.6% exposure frequency.

Two facts of anesthetic practice possibly can explain the high rate of exposure. Anesthesiologists as a group are in direct physical contact with the oral cavities of many more patients than other medical specialties. For example, the anesthesiologist may administer anesthesia to an average of five patients a day. Surgeons, on the other hand, perform an average of one procedure a day. Therefore, in 10 years of practice, while surgeons may have carried out procedures on 2,500 patients, anesthesiologists may have had exposure to 12,500 patients, a five times greater risk of exposure.

A second factor is that the anesthesiologist rarely isolates himself from his patient with the same rigor as his surgical counterpart. Direct contact with the patient is frequent and sustained. Human contact or human products constitute the major sources of viral infection. In many cases, the patient may not exhibit symptoms. Certain groups of patients, however, should be regarded as possible carriers. These groups have been identified as follows: all patients with liver disease, however acute or chronic; patients undergoing hemodialysis, or who have had a renal transplant; all patients with leukemia, lymphoreticularoses, polyarteritis nodosa, or polymyositis; patients being treated with radiotherapy or immunosuppressive drugs; immigrants or visitors from countries with a high background of carriers; persons who have been transfused in, or recently returned from countries with a high background incidence (namely, tropical and subtropical areas and Greenland); patients who have received blood or a blood product in the last 6 months or who have been transfused with blood or blood products from paid blood donors; inmates of prisons or institutions for the mentally defective; drug addicts; prostitutes; homosexuals; and persons who have been tattooed.

The hepatitis viral particle exhibits physical characteristics that encourage long-term survival. This virus can survive for 4 hours at 60°C and at room temperature for 6 months. It is resistant to phenol and chlorine-containing disinfectants. Heat or steam sterilization is best for both inactivating the virus and destroying its antigenicity. Hepatitis B surface antigen has been recovered from stainless steel surfaces, cotton swabs, dialysis unit panels, needles, needle clippers, and gloves. In one study, the exposure of hepatitis B surface antigen positive blood to stainless steel surfaces and cotton swabs at 25°C and 42% relative humidity, for 72 hours, resulted in only a 15–20% loss of antigenic activity; after 14 days, antigenic activity was reduced by another 15–20%. Recovery of hepatitis B antigen from the stainless steel, using the swab-rinse technique, was 100% effective. In the same study, no reduction of hepatitis B surface antigen was detected with six contaminated cotton swabs that had been in the mail for 7 days. These experiments demonstrate that much of the equipment and the instruments used by the anesthesiologist are potential fomites for hepatitis B virus.

The most frequently reported source of infection is contact with contaminated blood, although one study concludes that saliva is probably the main vehicle of infection in nonparenterally acquired type B hepatitis. Urine and feces are not significant vehicles of transmission of hepatitis B virus.

With the prevalence of hepatitis B, its many modes of spread, and ease of transmission, active preventive measures are extremely important. The facets of prevention encompass preoperative blood-screening policies, environmental sterilization, prophylactic immunization, and adherence to sterile procedure and garb.

**Preoperative Blood Screening**

Reducing the incidence of nosocomial hepatitis B virus would be a much easier task if the identity of hepatitis B virus carriers were known. Until recently, blood testing was limited to the detection of hepatitis B surface antigen as indication of infection. The most sensitive of tests, however, identified only about 50% of the units of blood that would transmit hepatitis B virus to patients. However, recent discoveries regarding the structure of hepatitis B virus and other associated antigen–antibody reactions have made hepatitis B screening much more reliable. Tests now can detect hepatitis B surface antigen, antibody to hepatitis B virus, the "e" antigen, and deoxyribonucleic acid polymerase activity, all markers of hepatitis B virus infectivity during the different stages of infection. In particular, the discovery of the hepatitis B core antigen and its antibody have led to the development of more reliable blood testing. This is because of the sequence of appearance of the antibodies; both antibody to hepatitis B virus and antibody...
### Table 2. Serologic Methods for Detecting Inapparent Hepatitis B Virus Infection

<table>
<thead>
<tr>
<th>Serologic Marker</th>
<th>When Detected after Exposure</th>
<th>General Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>18–84 days</td>
<td>Persists 14–148 days; identifies only 50% of blood units capable of transmitting HBV; in chronic HBV infection persistence is greater than 6 months</td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>&gt;165 days</td>
<td>May be produced in low concentration throughout acute stages of hepatitis B; Not detected in chronic HBV infection</td>
</tr>
<tr>
<td>HBeAg</td>
<td>18–84 days</td>
<td>Transiently detected</td>
</tr>
<tr>
<td>Anti-HBc</td>
<td>60–150 days</td>
<td>High titer during onset, persists in decreasing titer for many years, true marker for HBV infection</td>
</tr>
<tr>
<td>DNA polymerase</td>
<td>18–84 days</td>
<td>Transiently detected</td>
</tr>
<tr>
<td>e Antigen</td>
<td>18–84 days</td>
<td>Detected in individuals with circulating HBsAg and anti-HBs</td>
</tr>
</tbody>
</table>

* HBsAg = Hepatitis B surface antigen; anti-HBs = antibody to HBsAg; HBeAg = Hepatitis B core antigen; anti-HBc = antibody to HBeAg; Anti-e = antibody to e antigen; HBV = Hepatitis B virus.

Preoperative serotyping should be done on high-risk patients, checking for both hepatitis B surface antigen and antibody to core antigen. This “double screening” reveals both subclinical states, the prodromal period, and the symptomless chronic carrier. The patient whose results are negative for surface antigen, positive for antibody to core antigen, and negative for antibody to surface antigen should be treated as a hepatitis B carrier.41

### Prophylactic Immunization

Protection with immune serum globulin after known inoculation has been successful and more recently hepatitis B immune globulin has been used.42–45 In a study done to determine the efficacy of each in preventing hepatitis B after known exposure to hepatitis B virus, hepatitis B immune globulin was significantly more effective than immune serum globulin in reducing the incidence of both overt type B hepatitis and of type B infection. This suggests that the hepatitis B immune globulin blunts the effect of introduced hepatitis B surface antigen sufficiently to prevent active immunization.44 In another study, immune serum globulin was shown to afford partial protection against type B hepatitis.42 Immune serum globulin also was demonstrated to be superior to hepatitis B immune globulin in producing passive–active immunity and therefore is of potentially greater benefit in protecting persons working in high-risk environments.46 The ratio of overt disease to subclinical infection was the same in hepatitis B immune globulin recipients as it was in the immune serum globulin recipients. Thus, the achievement of a higher frequency of passive–activity immunity in immune serum globulin recipients was at the price of a higher frequency of overt Type B hepatitis. This hardly permits the designation of immune serum globulin as an effective prophylactic agent against Type B hepatitis.46 On the basis of work done by Seeff and others, it is quite apparent that hepatitis B immune globulin is superior to immune serum globulin as a prophylactic agent for type B hepatitis following known exposure to hepatitis B virus.45

There are no definite contraindications to the use of immune serum globulin or hepatitis B immune globulin, and they both appear to be safe for use in pregnant women.45 Because of the possibility of causing immune-complex disease, hepatitis B virus carriers should not be given hepatitis B immune globulin.43 Adverse reactions to immune serum globulin are uncommon when it is administered by the recommended intramuscular or subcutaneous routes.43

The most recent advance in the prevention of hepatitis B is the development of the vaccine, the use of...
which looks promising.40,45,46 Our hospital took part in a high-risk-staff immunization program, including surgical staff, anesthesiologists, laboratory personnel, and hemodialysis staff.

The hepatitis B vaccine is made using hepatitis B surface antigen harvested from chronic carriers by plasmapheresis. The acceptance of the vaccine has been slowed by concern regarding the possibility that the vaccine could be one of the unknown routes for the transmission of acquired immune deficiency syndrome. The vaccine is given in a series of three injections: two at an interval of a month and a booster shot at 6 months. It is estimated that the vaccine will protect a person for approximately 5 years at a cost of $110. In prelicensure trials, there were no statistical differences between the side effects from the vaccine and from a placebo.46

Based on the known properties of hepatitis and the recent advances in hepatitis B prophylactic measures, guidelines can be established for anesthesiologists, and adherence to such should eliminate the nosocomial hepatitis B virus infections transmitted between anesthesiologist and patient (table 3).

**Non-A/Non-B Form of Hepatitis**

The non-A/non-B form remains enigmatic; its clinical features resemble those of hepatitis B and it occurs most frequently after blood transfusions, but it also occurs after accidental needle sticks and close contact with a carrier. Diagnosis of non-A/non-B by serotyping is not yet possible, and so the diagnosis of non-A/non-B is made through a process of exclusion.10,28,37

**Herpesvirus**

Herpes simplex virus is a common infectious agent of humans.48 While acquisition of initial infection is usually oral, breaks in the mucous membrane or skin serve as a portal of entry. The virus remains with the individual throughout life in a dormant form residing in the sensory ganglia that innervate the site of primary infection.48 Various stimuli will reactivate the virus, which will reappear near the site of original infection or track along the nerves to remote sites. Because neutralizing antibody already is present, a four-fold antibody rise usually is not demonstrated during reactivation.

A wide range of nosocomially acquired herpesvirus infections has been reported, including herpetic infection of the digits (whitlow), herpes neonatorum, whitlow with encephalitic symptoms, acute gingivostomatitis, and acute diphtheria-like membranous pharyngitis.49,50 Both herpes simplex type I virus and type II have been implicated in these infections, and herpetic whitlows resulting from type II can contaminate and subsequently infect the genital area. Transmission has occurred from patients to staff and vice versa. Anesthesiologists are particularly susceptible to herpetic whitlow because of sustained direct contact with oral, tracheal, and pharyngeal secretions. Despite the extremely painful situation, with paronychial or pulp involvement, it has been stressed that treatment should not include surgical intervention.50 Attempts at draining cause the iatrogenic entrance of virus into the deep pulp space, often leading to serious complications such as secondary bacterial infections. Because this condition is self-limiting, infected anesthesiologists must refrain from dealing with the chronically ill, debilitated, or immunosuppressed patient until the lesions have evolved into the dry and crusting stage.

Recently, herpes type I virus has been found in the tracheobronchial secretions in 14 of 46 patients having adult respiratory distress syndrome.51 The control group which had been intubated and on ventilators but had no acute adult respiratory distress syndrome, were found to have negative test results for type I herpes simplex virus. This association has not been seen before. Additionally, mortality in the acute adult respiratory distress syndrome group was significantly higher in those patients having no antibody titer rise as compared with those with a large titer rise. At postmortem examination, type I herpes simplex virus was found in the vaginal ganglia, and the possibility exists that infection of

**Table 3. Guidelines for Hepatitis B Prophylaxis an Alternative to Hepatitis B Vaccination**

<table>
<thead>
<tr>
<th>I. Routine Serotesting</th>
<th>II. Exposure to Hepatitis B</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Seronegative personnel screen every 3–6 months for HBsAg* and Anti-HBs</td>
<td>a) report accident to employee health service</td>
</tr>
<tr>
<td>b) Anti-HBs positive personnel: test annually for anti-HBs and to confirm continued immunity</td>
<td>b) serologic testing of patient and employee for HBsAg</td>
</tr>
<tr>
<td>c) HBsAg positive personnel: test quarterly for antigen and anti-HBs when they become seronegative</td>
<td>c) Hepatitis B immunoglobulin administered only after type of exposure has been well documented and patient is antigenemic (administer within 7 days of exposure, preferably 24–48 hours)</td>
</tr>
</tbody>
</table>

the respiratory tract occurs secondarily to vagal ganglionitis.

Vidarabine (adenine arabinoside), a nucleoside derivative originally developed as an anticancer agent, is now being used to treat herpes.\textsuperscript{52,53} Clinical trials of this drug in groups of immunocompromised patients with zoster, patients with herpes simplex encephalitis, and in cases of neonatal herpes simplex infection have shown much improvement, including reduced mortality.\textsuperscript{53} Topical preparations are available and have been successfully used in corneal ulcers resulting from herpes; however, topical vidarabine has not proved useful in labial or genital forms of herpes infections.\textsuperscript{52}

Acyclovir is another antiviral drug gaining increasing acceptance.\textsuperscript{54–56} This drug has been used successfully in clinical trials to treat mucocutaneous herpes simplex virus infection after marrow transplantation. It has been shown to be a potent inhibitor of type I and II herpes simplex virus replication.\textsuperscript{57}

Treatment with the new generation of antiviral drugs such as acyclovir, vidarabine, and transfer factor may decrease the morbidity of these patients. At present, development of successful vaccination against human herpesviruses is unlikely.

**Varicella**

Another of the members of the family, *Herpetoviridae* is the varicella–zoster virus.\textsuperscript{58} The route of infection differs from herpes simplex in that the upper respiratory tract mucosa usually is the involved area. While most anesthesiologists have had childhood varicella, there may be some individuals that are not immune. The complication rate occurring with adult varicella disease is much higher than the childhood disease. Varicella pneumonia occurs in 2–30% of adult cases.

The most extensive epidemiologic study of nosocomial varicella infection took place at another hospital on the Harvard Medical School campus.\textsuperscript{59} The index patient, a 3-year-old child who had transverse myelitis had chicken pox develop. After 8 days of intensive care, she died of varicella pneumonia. Subsequent to her death, chicken pox occurred in 13 children and two adults. Airborne transmission of droplet nuclei was implicated strongly after analysis of airflow patterns using sulfuric acid smoke puffs, oil of wintergreen, and sulfur hexafluoride. It was determined that airflow from the index patient’s room was mixed with hallway air supply in ducts and was transmitted to other patient rooms. In addition, high vacuum air conduits were faulty.

**Adenovirus**

Adenoviruses derive their name from the fact that they were first isolated from adenoid tissues and they have an affinity for lymph glands where they may remain dormant for years. There are about 30 serotypes of adenoviruses. In addition to the adenoids, adenoviruses invade the respiratory tract, the gastrointestinal tract, and the conjunctiva.

Most adenovirus infections occur in children or in certain semiclosed populations like military recruits.\textsuperscript{60,61} There are three commonly seen syndromes associated with adenoviruses. Febrile acute respiratory disease (ARD), characterized by sore throat and cough, is seen in approximately 5–10% of United States military recruits.\textsuperscript{61,62} This syndrome is seen only sporadically in civilian populations.\textsuperscript{63} Pharyngoconjunctival fever is a syndrome characterized by pharyngitis, conjunctivitis, and fever that usually affects children and young adults. Epidemic keratoconjunctivitis often is an iatrogenic disease spread via ophthalmologic instruments, ointments, and contaminated fingers.\textsuperscript{64–66}

The anesthesiologist should be aware that there have been outbreaks of pharyngoconjunctival fever and keratoconjunctivitis reported among hospital personnel.\textsuperscript{64,67,68} In one case, abandonment of isolation procedures may have led to the outbreak,\textsuperscript{59} while in another\textsuperscript{67} a contaminated ophthalmic solution caused the outbreak. When working with patients known to have adenoviral disease, simple measures such as frequent handwashing and use of gloves should lessen such iatrogenic morbidity to patients and staff.

**Respiratory Syncytial Virus**

Respiratory syncytial virus belongs to the family *Paramyxoviridae* and constitutes one of three genera, the others causing measles (*Morbillivirus*) and mumps (*Paramyxovirus*). Its name is derived from the multinucleated giant cells observed in serially propagated human cell cultures (syncytial effect). It is the agent most responsible for infant pneumonia and bronchiolitis.

There have been numerous reports of large hospital outbreaks of respiratory syncytial virus in pediatric wards, as well as in newborn and pediatric intensive care units.\textsuperscript{70–76} Attack rates vary widely. Hall observed a rate of 119 cross-infections in infants per million susceptible days per infective day.\textsuperscript{75} Other studies using the same epidemiologic terminology have obtained rates as low as 32 cross-infections per million susceptible days per infective day.\textsuperscript{72} The nosocomial spread of respiratory syncytial virus also is dependent upon the design of the ward. Cross-infection was considerably higher in wards that lacked isolates that were physically separate from one another.\textsuperscript{75} Another factor was age. Younger children and infants were more susceptible to infection. Hall is emphatic about the role the staff plays in transmission. In her study, 10 of 24 staff members (42%)
acquired respiratory syncytial virus infection. In a later study, 56% of staff members became infected, with 82% showing symptoms of respiratory syncytial virus. Among those infected were 25 nurses, 10 physicians, and eight medical students.

It has been hard to demonstrate long-term viability of viruses in aerosols or contaminated fomites. Hospital personnel act as transmitters of infection to children by carrying contaminated secretions on their hands and clothes.

Methods of control include the isolation of infected infants; adherence to strict handwashing, gowning, and gloving; and, where possible, the temporary assignment of staff to either clean or infected areas. Anesthesiologists have not been implicated as yet in the transmission of respiratory syncytial virus.

**Influenza**

Influenza strikes both staff members and patients during seasons when the disease is present in the community. The most important reservoir of viral particles is the nasopharyngeal secretions of infected persons. Thus, the anesthesiologist can have frequent contact and be responsible for spread of influenza among the surgical population. In addition, infected staff with subclinical infection can transmit the virus directly to susceptible patients. Of course, patients can acquire influenza from patients newly admitted with influenza, patients who develop nosocomial influenza, and visitors.

Influenza disease may lead to increased tracheobronchial colonization with bacteria. Airway colonization with these organisms frequently results in pneumonia. Studies are now indicating that influenza causes extensive damage to the tracheobronchial tree, particularly to the mucosal surfaces. The resulting desquamation of the upper airway exposes basement membrane surfaces that selectively adsorb gram-negative organisms such as *Pseudomonas aeruginosa*. The increased bacterial load, together with an impaired mucociliary transport system, promotes colonization. The presence of an endotracheal tube allows contaminated secretions to pool on the surface of the cuff. In this situation, pneumonia is likely.

The risk of influenza to patients is reduced by vaccinating the staff. Studies have indicated that less virus is shed in the nasal secretions of vaccinated personnel. In 1976, Guillain-Barré syndrome appeared in excess frequency among persons who had received the A/New Jersey/76 swine influenza vaccine. There were 10 excess cases for every million persons vaccinated. In subsequent vaccination programs, the incidence of Guillain-Barré syndrome is not significantly higher than in the unvaccinated population. The other form of protection is the prophylactic use of the drug amantadine hydrochloride. This drug is indicated only for influenza A. Use of amantadine has shown an 80% reduction in attack rate with prophylactic use. In addition, patients with uncomplicated influenza not requiring hospitalization for other reasons should not be admitted.

**Parainfluenza Viruses**

The parainfluenza viruses are exceeded only by respiratory syncytial virus as important causes of lower respiratory disease in young children. To a much lesser extent, they also may produce upper respiratory illness in older children and adults resulting from reinfection. There are four known parainfluenza virus types. Types 1 and 2 are the principle cause of croup (laryngotracheobronchitis) in children. Type 3 is second only to respiratory syncytial virus as a cause of pneumonia and bronchiolitis in infants younger than 6 months of age. Type 4 is a frequently isolated and relatively innocuous strain.

The parainfluenza viruses possess a high degree of infectivity. Transmission of parainfluenza viruses occurs by direct person-to-person contact or by large droplet spread. In some studies, approximately 90% of children have antibodies to the Type 3 virus. Others have shown that about 50% of children possess antibodies to Type 1 and 2 viruses. Although the parainfluenza viruses infect a large segment of the population, Types 1 and 2 rarely produce serious disease. However, Type 3 is a significant cause of respiratory disease, especially pneumonia and bronchiolitis, that primarily affects infants in their first months of life. Because of the mode of transmission, medical personnel appear to have a low probability of cross-infecting other patients unless they are infected with parainfluenza.

**Rhinovirus**

Ellis has addressed the relationship of anesthesia to the common cold. He postulated that under most conditions, the patient who has mild upper respiratory tract infection should not be prevented from having a surgical procedure including general anesthesia. The exceptions might be patients who will be subjected to abdominal or hernia procedures who might put the incision at risk by coughing; however, anesthetic and surgical management should be modified to lessen the risks of coughing. Of course, the conservative approach is to postpone the operation until the illness and its symptoms have been resolved. The perioperative and postoperative course of children presenting for myringotomy and typanostomy who had upper respiratory viral infection at time of operation was investigated re-
ently.\textsuperscript{98} Cohorts of similar patients with either no evidence of viral infection or questionable evidence were included. In the first 73 patients, all of whom had halothane/O\textsubscript{2}/N\textsubscript{2}O administered by face mask, there were no complications seen after operation in any patients regardless of the presence of uncomplicated upper respiratory infection. It would seem that general anesthesia for minor operation need not be postponed if the patient has an uncomplicated upper respiratory infection and if endotracheal intubation is not considered necessary. In influenza-infected ferrets, anesthesia with halothane, diethyl ether, or pentobarbital did not seem to increase the severity of disease. These findings are based on criteria including temperature increase, lethargy, rhinorrhea, and tissue abnormalities upon necropsy.\textsuperscript{99} In infected ferrets who had enflurane anesthesia, increased histopathologic changes were observed.

Rhinovirus can be easily transmitted.\textsuperscript{100-102} In these studies, rhinovirus, which causes one-third or more of adult common colds, is not transmitted by the airborne route but rather by inoculation from contaminated environmental surfaces or from the skin of infected individuals. In only two of 25 infected persons was virus expelled in a cough or sneeze.\textsuperscript{101} Virus was more likely to be found on the skin. Rhinovirus survives well on inanimate materials such as formica, stainless steel, nylon, and dacron. In more recent studies, rhinovirus infection could be transmitted by hand-to-hand contact significantly more effectively than small or large particle aerosols, a convincing argument against indiscriminate hand-shaking.\textsuperscript{100} Rhinovirus infection could be effectively interrupted by application of 2% aqueous iodine to the tips of the fingers.\textsuperscript{103} The effectiveness of inhibition lasted up to 2 hours. Anesthesiologists who have colds might use this method, although the cosmetic properties of 2% iodine discourage one against doing this.

With regard to seasonal prevalence, anesthesiologists can expect to see increased numbers of patients who have upper respiratory tract and airway infections resulting from the adenoviruses, respiratory syncytial viruses, influenza, parainfluenza, and rhinoviruses beginning in the late autumn and lasting until early spring. Epidemics resulting from these viruses will occur during these colder seasons.

Rubella

The teratogenic complications of rubella are well known. Transmission of this 60 nm ribonucleic acid virus is accomplished via the airborne route, and the virus manifests itself as a posterior auricular and suboccipital lymphadenopathy in susceptible individuals. Much subclinical infection also occurs. Transmission of rubella virus from hospital personnel to patients and vice versa is an unfortunate situation and has been reported in the literature as large-scale outbreaks that result in much lost work time and tremendous expense in both searching out susceptible individuals and instituting mass immunization programs.\textsuperscript{104-108}

While rubella infection in obstetric–gynecologic personnel may have serious consequences to their pregnant patients, anesthesiologists can readily participate in the chain of transmission. Seventy per cent of individuals in the United States that contract rubella are 15 years or older. This includes women of child-bearing age, 20% of whom probably are susceptible.\textsuperscript{109}

The prevention of rubella epidemics seems straightforward enough until the hospital health service tries to implement the program. The first step, of course, is to determine in all employees, male and female, who is susceptible. Those found susceptible are urged to become vaccinated. The vaccine, available since 1969, is a live rubella virus vaccine prepared in human diploid cell culture. It is provided as a monovalent, divalent (measles-rubella), or trivalent (measles, mumps, and rubella) vaccine.\textsuperscript{109} Immunity acquired as a result of vaccination is probably lifelong. Side effects and adverse reactions are minimal. In most reports describing nosocomial rubella outbreaks and the resulting vaccination program, compliance ranges from high to low, the low compliance rate being consistently the physician population.\textsuperscript{108,110} Whose failure to implement disease-preventing behavior probably is related to lack of perceived vulnerability and the press of other priorities. This is unacceptable when pregnant women constitute the patient population. Since 1979, our institution requires new employees and physicians to provide written assurance of rubella immunization.

Creutzfeldt–Jakob Disease

Creutzfeldt-Jakob disease is a subacute degenerative disease of the central nervous system typified by progressive pre-senile dementia.\textsuperscript{111-114} The incubation period in the three probably iatrogenically transmitted cases has been as short as 17–18 months.\textsuperscript{115,116} There is no known treatment. Creutzfeldt-Jakob disease almost always leads to death within 6 months of onset. The disease is caused by a transmissible virus that is membrane associated, has unusual resistance to physical and chemical means of inactivation, and has not been shown to induce any detectable immune reaction.\textsuperscript{117} Although it is not a common disease, it also is not exceedingly rare. There are, for example, more cases of Creutzfeldt-Jakob disease in the world than there are cases of rabies. A genetic factor related to susceptibility cannot be discounted.
Experiments designed to study the modes of transmission have been limited, of course, to nonhuman primates, where transmission has been accomplished by several routes. Of concern to the anesthesiologist is the fact that the disease was transmitted successfully through the oral route using infected brain. There have been only two reported instances of nosocomial infection. One involved a patient who had a corneal transplant. The second involved two patients who underwent procedures using contaminated stereotactic electrodes. In our institution, a ward secretary and a nurse received needle puncture injuries from an uncapped syringe containing material aspirated from a cranial fluid collection of a patient known to have Creutzfeldt-Jakob disease. After 2 years, neither shows signs of the disease.

Anesthesiologists should be aware that contact with blood, cerebrospinal fluid, and nervous tissues might increase the risk of transmission. The risk is slight, but to take care during brain biopsies for dementia is prudent because a firm clinical diagnosis of the subacute spongiiform encephalopathies is difficult to establish. In 308 patients with Creutzfeldt-Jakob disease studied by Gadjusek, 18 were in health-related professions, including two physicians, one pediatric neurosurgeon, four dental surgeons, and seven nurses. To date, the disease has not been reported in any pathologist, anesthesiologist, mortician, or morgue attendant.

Contaminated material has been adequately disinfected with 0.5% sodium hypochlorite (10% chlorox) as well as steam and ethylene oxide sterilization. Before linen and instruments known to be contaminated leave the operating room, they should be soaked in 1% sodium hypochlorite and properly bagged and labeled. Two hundred and sixty-nanometer ultraviolet irradiation, ionizing radiation, 3–10% formalin, and 70% ethanol fail to inactivate Creutzfeldt-Jakob disease virus. The disease, although not prevalent, is nearly always fatal. Adequate precautions should be taken by anesthesiologists, but because it is a disease of low contagion, anesthesiologists should not hesitate to give anesthesia to patients in whom the disease is suspected.

There is no evidence of hospital-associated transmission of the other slow virus diseases of humans including subacute sclerosing panencephalitis, caused by measles virus, and progressive multifocal leukoencephalopathy, caused by papova JC virus. In addition, the association of multiple sclerosis, amyotrophic lateral sclerosis, and Alzheimer's disease with a viral cause is under investigation.

Prevention of Viral Infection

The prevention and control of viral infection has been reviewed recently. We shall address specifically prevention of viral infection and specific guidelines for the protection of anesthesiologists and their patients. The importance of prevention is underscored by the fact that infection by many viruses is enhanced by the stresses imposed by surgery and anesthesia. While the exact mechanisms remain to be elucidated, there is general agreement that there is inhibition of phagocytic mobilization with subsequent depression of phagocytosis in the presence of anesthetics. Reduction in antibody-producing cells in the presence of halothane, nitrous oxide, and pentobarbital has been observed. Would this generalized depression of immunologic responsiveness exacerbate infections in patients harboring viruses or acquiring viruses during hospitalization? The limited work carried out so far seems to indicate that increased susceptibility is virus dependent, anesthetic dependent, and dose dependent.

Mouldgil studied mice infected with the murine hepatitis virus by intraperitoneal infection and exposed groups to 1.5% halothane or oxygen for 2 hours. The anesthetized groups had a statistically higher mortality when compared with the unanesthetized groups. Moreover, the LD₅₀ was reduced by a factor of 10 in the halothane-treated groups. In another study, by contrast, exposure of virally infected mice and dogs to diethyl ether lessened the severity of disease.

The most extensive in vitro studies on the effects of anesthesia on viral infection continue to be carried out by Knight et al. His initial studies dealt with the single-stranded ribonucleic acid paramyxo virus responsible for measles. In this study, cells of a continuous primate cell line were exposed to different concentrations of halothane: 0, 0.8, 1.2, 1.4, and 1.5% for various times up to 72 hours. A dramatic reduction in virus titer upon exposure to halothane was demonstrated. The reduction increased as the halothane concentration increased. There were no observable effects in terms of toxicity on the cell cultures themselves. At 1.5 and 1.8% halothane there was no virus replication. A decrease of viral-specific cytopathogenic effects also was seen. Furthermore, antiviral activity ceased when the halothane was removed.

To begin to elucidate the point in the virus life cycle where halothane exerts its effect, Knight's group examined viral adsorption to cells. Viral adsorption did occur during the presence of the anesthetic. Further investigation of the effects halothane had on the synthesis of viral nucleocapsids showed that inhibition did occur. Inhibition corresponded to reduction in infectivity. Tritiated uridine incorporation into the nucleocapsid was completely inhibited by 1.8% halothane. Synthesis was reinstated again when the anesthetic was removed, although defective virus particles possessing a smaller amount of genomic material were present.
The effect of halothane on virus protein and ribonucleic acid synthesis was investigated with use of virus specific immunofluorescent antisera. At halothane concentrations of 1.8%, measles virus-specific antigen was not synthesized. Viral ribonucleic acid synthesis also was found to be inhibited. Thus, the dramatic interference of halothane on the life cycle of this one virus seemed to indicate that inhibitory effects are exerted after viral adsorption but before ribonucleic acid synthesis.

Knight recently expanded his investigations to include other viruses including poliovirus and herpesvirus. The replication of this latter virus also was inhibited.\(^{132}\) Poliovirus and influenza A virus replication were unaffected by 2% halothane. Furthermore, investigation of other anesthetics, including enflurane and isoflurane, have shown a dose-dependent and reversible inhibition of measles virus replication as well as increased survival in influenza-infected mice.\(^{134}\)

Most recently this group has been able to show that viruslike particles released from halothane-treated herpes simplex virus-infected cells were found to be devoid of deoxyribonucleic acid.\(^{131}\) The finding of defective virus particles is important in that they have been shown to be possible etiologic agents for chronic central nervous system infections such as subacute sclerosing panencephalitis.\(^{135-137}\) However, we know of no evidence that panencephalitis is more common in patients who have undergone surgery and anesthesia.

**Physical Environment of the Anesthesia Machine**

No study has been undertaken to determine the fate that befalls viral particles expelled into the environment of the anesthesia machine. The physical properties of humidity, dessication, and temperature all affect virus survival. The effects of anesthetics on virus replication already have been addressed. Some pertinent extrapolation probably can be made on the basis of work carried on outside the field of anesthesiology.

In general, viruses do not survive in nature for prolonged periods of time outside a viable host. However, viral particles can remain viable on inanimate surfaces for a surprising period of time. This has already been discussed with regard to hepatitis B and the rhinoviruses.\(^{29,32,101}\) Influenza virus will probably remain viable for 24 hours within an anesthesia circuit, although viability will depend upon humidity.\(^{138}\) In this case, the lower the relative humidity, the greater the survival. Viruses deposited in anesthesia machines are subject to dessication and will undergo inactivation over time. Viruses exposed to temperatures normally associated with anesthesia probably will not become significantly less viable. In studies done with rhinoviruses, it was found that relatively few particles are expelled in aerosols of various magnitudes from coughing or sneezing.\(^{101}\) The reason for this is not understood altogether but may be associated with the innate intracellular characteristics of viruses. In contrast, bacteria that are primarily extracellular parasites are commonly associated with expelled aerosols from the upper airway.\(^{139}\)

In a general study of viruses as agents of airborne contagion, it has been demonstrated that large numbers of small particles, 10 \(\mu\)m minimum mean diameter, are produced by sneezes and coughs in nonrhinoviral virus upper respiratory infections and that virus can be recovered from these exhalations. Virus can be recovered from the air of rooms occupied by infected subjects. Small doses of virus are infectious by small particle aerosol. The demonstration of airborne infection with coxsackievirus A type 21 under controlled conditions also was noted.\(^{25}\)

Hepatitis B virus, for example, is small and can pass through a filter with a pore diameter of 52 nm.\(^{140}\) The role of particle size in transmission is important; to be effective in airborne transmission, particles should be small, about 10 \(\mu\)m in diameter or less, because small particles will remain suspended in air for periods long enough to permit their dissemination. Particles that are 1–3 \(\mu\)m in diameter will remain suspended almost indefinitely, especially if they are elevated periodically by air currents. Size also affects the amount of virus released by sneezes and coughs, with the greatest concentration being with particles of one \(\mu\)m or less in diameter. Coughs, sneezes, and other exhalatory activities produce large numbers of small particles that can then serve as vehicles of airborne virus transmission, especially because the small size facilitates wide dissemination. Favero’s study, referred to earlier, demonstrated the minimal loss of hepatitis B virus antigenicity in the constant conditions of an ambient environment.\(^{32}\) The indefinite suspension of hepatitis B virus, along with its antigenic stability, strengthens the position that hepatitis B can be transmitted by airborne spread.

The lack of expelled viral particles may be compensated for by the small number of viral particles needed to cause infection. Thus, even a small number of infectious particles may be enough to initiate clinical infection. An anesthesiologist handling an infected machine might lead to infection of a patient who subsequently receives an anesthetic from that machine. Investigations need to be performed to confirm or refute these possibilities. Until these studies are done, the role of the anesthesia machine in transmitting viral infection will remain in doubt.

**Disinfection and Sterilization of Equipment**

Table 4 summarizes the more commonly employed disinfectants and their effectiveness in inactivating the
viruses we have discussed. The quaternary ammonium compounds and alcohols seem to be less effective overall and probably should not be used. In addition, these compounds have a decreased effectiveness against certain gram-negative bacteria. The only virus that demands more stringent attention is the agent of Creutzfeldt-Jakob disease. One should use 0.5–1.0% sodium hypochlorite (e.g., 10% chlorox) for all disinfecting purposes involving Creutzfeldt-Jakob disease.

With regard to hepatitis, sterilization procedures need to be practiced because the hepatitis virus does not succumb to disinfection. Activated 2% glutaraldehyde has been demonstrated to be an efficient viricidal cold sterilizing agent. It is of relatively low toxicity; has a short sterilization period; has no observable deleterious effects on lensed instruments, metal, and metal thread components; and is effective for at least a 2-week period, during which time it can be reused. In the presence of formaldehyde, the helical structure melts at a relatively low temperature, freeing the amino groups. Autoclaving should be at 15 lb. per square inch at 121°C, boiling should be for at least 20 min, and heating in a sterilizing oven should be done at 180°C for 1 h. Ultraviolet light at 260 nm acts mainly on nucleic acids and is not well suited for viral inactivation because its damage to nucleic acids can be repaired by a variety of enzymatic and genetic mechanisms.

Ethylene oxide and steam sterilization kill all viruses.

**DISPOSABLE CIRCUITS AND FILTERS**

Unless the patient is known to have active hepatitis B infection, the use of disposable circuitry and filters cannot be either advocated or dismissed, with good conscience, because of the lack of scientific evidence. Use of these devices has been shown not to lessen postoperative bacterial pneumonia in controlled studies. Their use even may add a false sense of security, leading to decreased vigilance and increased failure to use more accepted disinfection methods.

**Personal Protective Measures**

Anesthesiologists should recognize that they provide an excellent means of transmission of viruses to patients and should be aware that although they can work through a day, the shedding of viruses from their mucous membranes and skin during viral infection may provide the inoculum to complicate the postoperative period of the patient. Rashess of any kind should be scrutinized before deciding to administer anesthesia. Viruses originating from the airway are more likely to be transmitted to hands and then to patients than by direct droplet transmission. Thorough handwashing is as important in preventing viral transmission as bacterial transmission. The use of gloves protects both patient and anesthesiologist alike. The greatest risk to the anesthesiologist is hepatitis B and herpes simplex infections, and the chance of infection with both can be lessened substantially by wearing gloves. A staff member with any herpes infection should not care for an immunosuppressed patient, a patient who has extensive burns, leukemia, or lymphoma, or patients on protective isolation.

Immunization against influenza, rubella, and now hepatitis are available for the protection of anesthesiologists and their patients. Anesthesiologists should ascertain their rubella titer and be immunized if found susceptible. Preemployment health screening should include a varicella history as well.

If outbreaks of viral infection do occur in the hospital,
anesthesiologists should be among the first to cooperate with isolation policies, mass immunizations, and other necessary measures. Studies on the management of viral outbreaks indicate a consistently low compliance among physicians in presenting themselves for immunization.109

Viral infections are a fact of hospital life. Anesthesiologists can play a crucial role in eliminating themselves as links in the transmission of viruses to patients and in so doing, improve their own chances for a long and healthy career.

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