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Detection of Viral Antigens, Particles, and Early Antibodies in Diagnosis

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Immunoassays for the detection of viral antigens in clinical specimens and virus-specific IgM responses in serum have shortened the time required to make a laboratory diagnosis of several infections. A range of antigen detection systems are available, varying in sensitivity, complexity, and expense, and each may have a role to play depending upon the laboratory setting. Technical advancements to eliminate false-positive results in solid-phase IgM assays have provided an awareness of very early IgM responses in diseases such as rubella, hepatitis A, and mumps. When clinical specimens contain large numbers of virus particles, a rapid diagnosis is easily made using electron microscopy. Detection of antigens, virus particles, and IgM responses is creating increased demands for viral diagnostic services in primary care settings. Other approaches using sensitive probes for viral nucleic acids or enzymes will also serve as viable laboratory techniques in the future.

DETECTION OF ANTIGENS

Table 1 summarizes several reported techniques for the detection of viral antigens. Gel diffusion, rheophoresis, and immunoelectrophoresis (IEOP) employ gels in which antigen and antibody move toward each other, resulting in a line of precipitation. Thin-layer immunoassay (TIA) involves the adsorption of a thin layer of globulins onto a polystyrene surface [1,2]. This surface then has the characteristics of an immunosorbent which is able to bind antigens. The antigen/antibody interaction is visualized on the plate by exposing it to water vapor. Immune complexes are hydrophilic and the background is hydrophobic; thus differences in condensation patterns are easily recognizable to the naked eye. Latex agglutination (LA), indirect hemagglutination inhibition (IHI) or reverse passive hemagglutination (RPHA), and solid-phase aggregation of coated erythrocytes (SPACE) [3] are all based on the principle of coating a visible marker such as latex particles or erythrocytes with antibody. These tests are usually performed by mixing specimens with the coated surfaces and allowing time for settling. SPACE is a solid phase variant of the test (Fig. 1). These tests are relatively rapid, sensitive, and simplistic. A commercially available LA test for rotaviruses has enabled the immediate processing of stool suspensions from children admitted to hospital with gastroenteritis during winter months when a large number of specimens are submitted to the laboratory (greater

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TABLE 1
Detection of Antigens in Clinical Specimens

GEL DIFFUSION
RHEOPHORESIS
COUNTER IMMUNOELECTROOSMOPHORESIS (CIEOP)
THIN LAYER IMMUNOASSAY (TIA)
LATEX AGGLUTINATION
SOLID PHASE AGGREGATION OF COATED ERYTHROCYTES (SPACE)
IMMUNOFLUORESCENCE (IF)
IMMUNOPEROXIDASE (IP)
RADIOIMMUNOASSAY (RIA)
ENZYME LINKED IMMUNOSORBENT ASSAY (ELISA)

than 15 per day) and routine electron microscopy (EM) becomes cumbersome. The LA test usually allows rapid identification of more than half of the infections and the negatives can be examined for other agents by EM.

Immunofluorescence (IF) and immunoperoxidase (IP) microscopy have been used for the detection of antigens in infected cells taken directly from the patient [4,5,6]. Specimens, after fixation, are stable and can be dispatched without time limitations because infectivity is not a factor. The test may be performed by a direct method in which antiviral antibody carries the fluorescent label, or an indirect method where an unconjugated antiviral antibody is detected by a labeled anti-species antibody. Either or both techniques may be used, depending upon the diagnostic situation. For example, if only one antigen is being sought, a direct method might be a better choice (i.e., herpes encephalitis) (Fig. 2). This patient, as well as several others, have yielded a positive identification of herpes simplex virus (HSV) antigens in brain biopsy before the administration of antiviral chemotherapy. Investigation of a patient with respiratory infection when several respiratory viruses may be circulating in the community would require the use of an indirect technique employing several an-

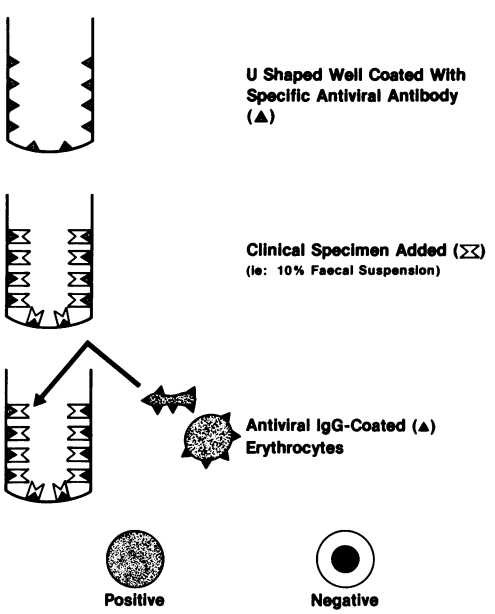

FIG. 1. Solid-phase aggregation of coated erythrocytes.

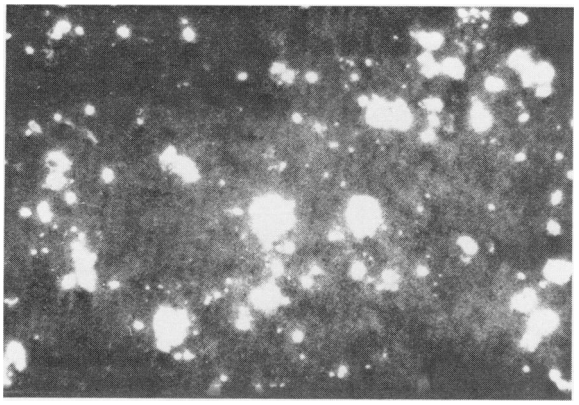

FIG. 2. Direct immunofluorescence of HSV-infected brain tissue.

tibodies (Fig. 3). The technique is dependent upon highly specific reagents, a fluorescent microscope, and a certain amount of expertise and patience. Its value has been demonstrated for the diagnosis of respiratory infections on admision to our pediatric wards but success is dependent upon collection of appropriate nasopharyngeal specimens containing infected cells.

Radioimmunoassay (RIA) and enzyme-linked immunosorbent assay (ELISA) are based on similar principles employing a solid phase coated with a capture antibody (CA) against a specific virus. Like IF microscopy, direct or indirect techniques have been developed [7,8]. RIA employs radioactively labeled anti-sera (i.e., iodine) and a gamma counter is necessary to read the results. The ELISA technique employs an enzyme attached to an indicator antibody (IA) which causes a color change when the appropriate substrate is added. This technique may be read by the naked eye or in a spectrophotometer, depending upon the quality and quantity of analysis that is required.

Solid-phase immunoassays (RIA and ELISA) are the most sensitive techniques available for the detection of antigens in clinical specimens. Their optimal use for rapid viral diagnosis appears to be in a situation where several specimens might be examined for an antigen in a given run. Most techniques require a day or overnight incubation to perform the test. Most of these techniques employ one of the three methods shown in Fig. 4: *(1)* competitive, *(2)* direct, or *(3)* indirect. In the competitive assay [9], enzyme-labeled antigen is mixed with the test sample containing

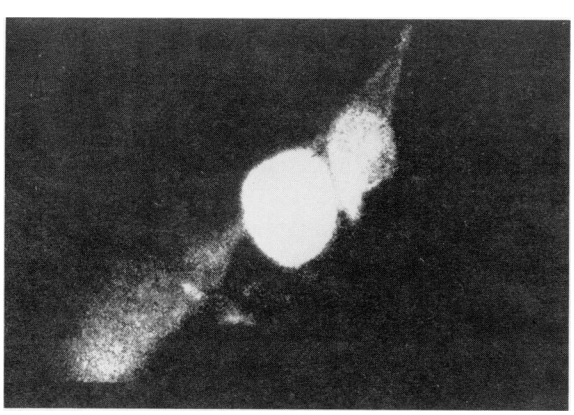

FIG. 3. Indirect immunofluorescence of throat washing infected with influenza A virus.

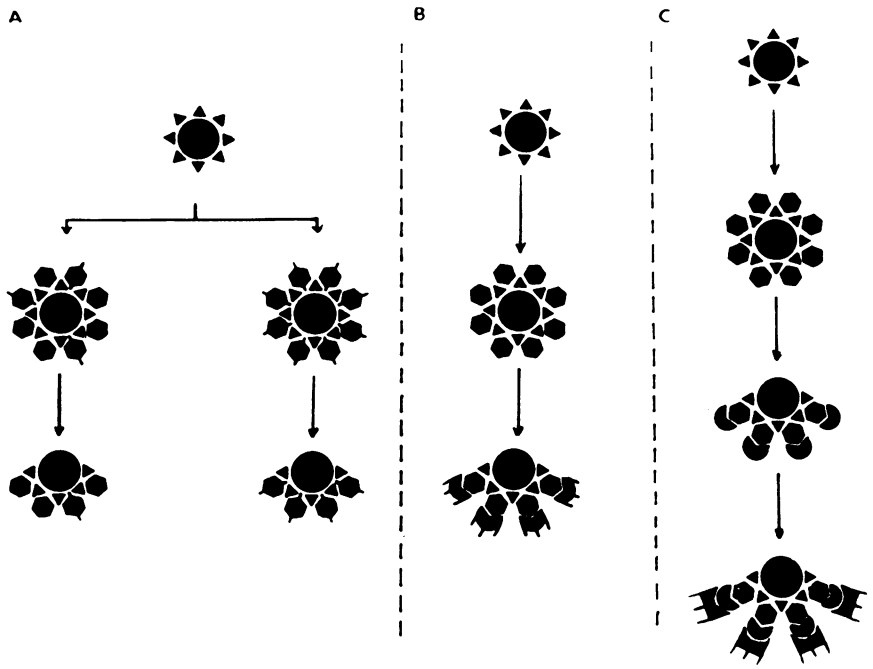

FIG. 4. Solid-phase immunoassays: **A** competitive; **B** direct; **C** indirect. ● Solid phase; ▲ Capture antibody or antigen; ⬣ Antigen or antibody in clinical specimen; ◖ Detector antibody; ⧗ Indicator antibody conjugated; ⧗ Conjugated detector antibody; ⬣ Conjugated competitive antibody or antigen.

antigen, which competes for a limited amount of antibody attached to the solid phase. Unbound antigen is washed away and the difference in indicator activity between the specimen and the control is compared. In a direct assay the clinical specimen is added to a solid phase which has a CA attached to it. Unbound antigen is washed away before the addition of conjugated detector antibody (DA). The indirect test is similar to the direct assay employing a CA and DA, but the DA is not conjugated. Instead, a third conjugated IA, which is anti-species to DA, is used. This approach has become popular for ELISA because of the availability of IA enzyme conjugates from commercial sources. A number of solid phases have been used, including test tubes, microtiter plates, beads, filter paper discs, and resins. The type of solid phase will dictate the kinds of instrumentation to be used in manipulation of the various steps in the procedure. Immunoassays have been successfully applied for the detection of hepatitis A virus (HAV) [10], hepatitis B virus (HBV) [11], rotavirus [12,13], adenovirus [14,15], herpes simplex virus (HSV) [16,17], respiratory syncytial virus (RSV) [18], influenza A virus [19,20,21], cytomegalovirus (CMV) [22], and Coxsackie viruses [23,24], and commercial kits are becoming available for several. Table 2 shows a small comparison of the ability of EIA and electron microscopy (EM) to detect rotavirus in stools from patients with gastroenteritis. Thus we have used EIA for rotavirus antigen detection in clinical specimens to facilitate processing large numbers of specimens as cited above employing LA.

Recently, hybridoma technology has enabled the use of monoclonal antibodies in

TABLE 2
Comparison of Direct Electron Microscopy (EM) and Direct Enzyme-Linked Immunosorbent Assay (ELISA) on Feces from Patients with Gastroenteritis, Hamilton, Canada, 1982

Specimens	Electron microscopy		Direct ELISA*	
	Positive	Negative	Positive	Negative
120	100	20	103**	17

* Rotazyme (Abbott Laboratories, N. Chicago)

** Three ELISA positive/EM negative specimens were positive by EM after reacting with rotavirus antiserum.

these assays. Using polyclonal CA and group- and type-specific monoclonal antibodies to HSV as detector reagents, we were able to establish cutoff values (.05 or .025) in an ELISA test which identified a virus isolate as HSV (Fig. 5). By constructing optical density ratios with the reactions to the two monoclonals (Fig. 6) all isolates falling above 1.5 were type 1 and below were type 2. In a comparison with an IF technique and restriction endonuclease analysis the ELISA test was 100 percent sensitive and specific for identification and typing (Table 3). Thus this methodology enables us to obtain a more rapid diagnosis when needed by assaying infected cell culture fluids after 24 hours' incubation and providing virus typing at the same time. The assay's sensitivity on clinical specimens, however, was only 78 percent of that on tissue culture positives.

DETECTION OF EARLY ANTIBODY RESPONSES

Early antibody (IgM) responses may be detected relatively rapidly after the onset of symptoms in some infections. Traditional techniques for their separation and measurement are shown in Table 4. Density gradient centrifugation and column

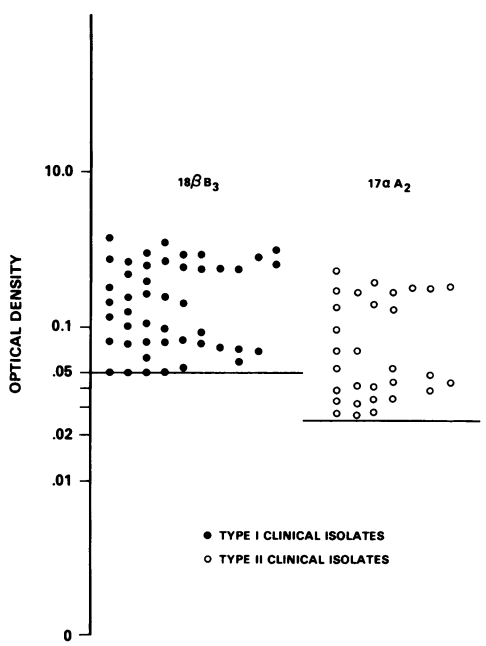

FIG. 5. Establishment of cutoff values for identification of HSV employing monoclonal antibodies in an enzyme immunoassay.

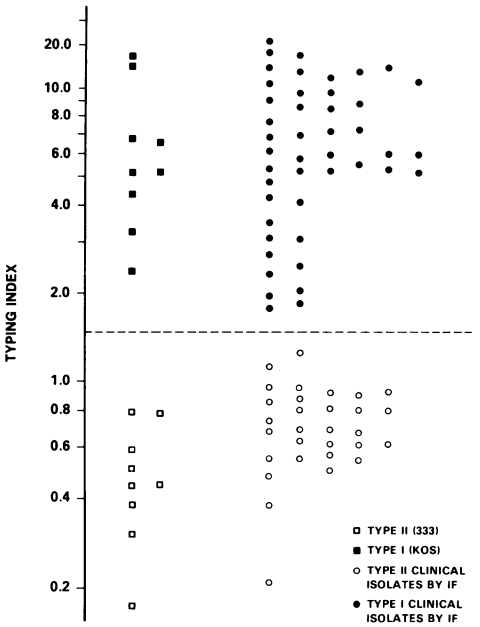

FIG. 6. Typing indexes used for identification of HSV isolates.

TABLE 3
Identification and Typing of HSV by Immunofluorescence (IF), Enzyme Immunoassay (EIA), and Restriction Endonuclease (RE) Analysis

	IF	EIA		RE Analysis
		Identification	Typing	
HSV Type I	45	45/45	45/45	22
HSV Type II	30	30/30	30/30	14
TOTALS	75	75/75	75/75	36

TABLE 4
IgM Antibody Measurement

SEPARATION
- Sucrose density gradient
- Gel filtration
- Staphylococcal protein A
- 2-mercaptoethanol

DETECTION
- Hemagglutination inhibition
- Electrophoresis
- Radioimmunoassay
- Enzyme linked immunosorbent assay
- Etc.

TABLE 5
Solid-Phase IgM Assays
(Separation and Detection in the same Test)

Immunofluorescence
Radioimmunoassay
Enzyme immunoassay
Erythrocyte indicators (SPIT, SPRIST, HIT)
Immunosorbent Agglutination Assay (ISAGA)

chromatography are probably the most accurate means available for the separation of IgM. However, these techniques are relatively complex, time-consuming, and expensive to perform. Consequently not many laboratories would employ them on a routine basis. Absorption of the serum with a preparation of staphylococcal protein A (SPA) has been used with varying success for the detection of rubella-specific IgM in order to diagnose recent infection [25]. Similarly, 2-mercaptoethanol has been used to destroy IgM in sera. A comparison is then made of treated and non-treated sera for the measurement of antibody responses. Both of these techniques, although easy to perform, have their problems with specificity of reaction. The products of separation in any of these methods are usually assayed in standard tests such as hemagglutination inhibition (HAI), RIA, ELISA, and so on.

There is a trend toward the development of assays which will separate and measure in the same test (Table 5). IF was one of the earliest approaches to IgM measurement using infected cells to trap IgM from serum [26–29]. This approach has the difficulties of creating a uniform expression of antigens and elimination of adsorption of immunoglobulins to Fc receptors expressed on the surface of virus-infected cells. Thus more recent approaches use inanimate solid phases (see section on antigen detection) and indicators conjugated with isotopes, enzymes, erythrocytes, or latex particles. Figure 7 illustrates the principles of IgM measurement using a capture antigen on the solid phase. The antigen may be adsorbed

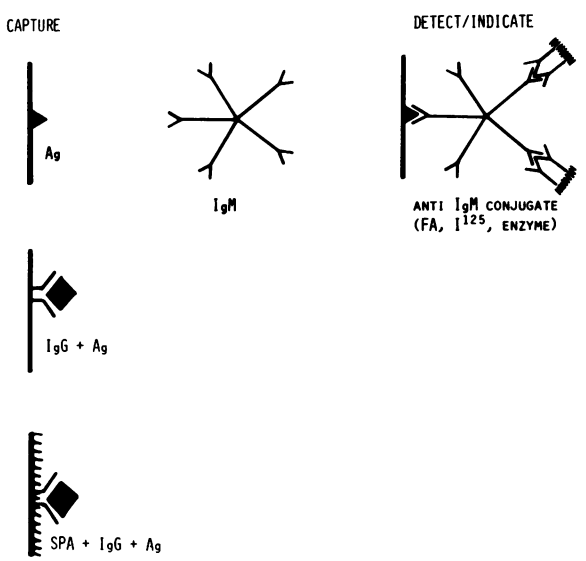

FIG. 7. Solid-phase IgM assay employing capture antigen.

directly or stuck to the solid phase with immunoglobulin or a combination of immunoglobulin and SPA. Captured IgM is then indicated by an anti-IgM conjugate (direct test) or through an indirect method. Table 6 summarizes most of the capture antigen IgM systems that have appeared [30–43]. Most of the publications have appeared on Epstein-Barr virus (EBV), CMV, and rubella virus. For the diagnosis of rubella, it is now possible to employ sensitive and specific IgM ELISAs on a single serum. Thus we have incorporated this test into our serological battery of tests on patients presenting with signs and symptoms compatible with rubella and on others whose serological profile contain a negative rubella PHA response and a positive hemagglutination inhibition or ELISA (IgG) response. Renal allograft patients are investigated in our laboratory for primary or reactivated BK papovavirus (BKV) infection by testing serum for BKV IgM antibody using a capture antigen RIA.

Figure 8 illustrates specific IgM detection employing antibody to IgM on the solid phase. This captures all IgM from the serum, but the specific viral IgM can be targeted by the subsequent addition of viral antigen. The presence of trapped antigen is then indicated (direct or indirect) by a conjugate. If the viral antigen has the

TABLE 6
Publications on Solid-Phase Capture Antigen IgM Assays

Virus	IFA	RIA	EIA
Epstein Barr	Schmitz (1972,78) Joncas (1975) Sumaya (1982)		
Coxsackie B		Dorries (1980)	Dorries (1983)
Cytomegalo-virus	Hanshaw (1968) Schmitz (1977) Robertson (1977)	Knez (1976) Kangro (1978,80,82) Jankowski (1980)	Schmitz (1972,77) Cappel (1978) Ziegelmaier (1981)
Dengue			Dittmar (1979)
Echovirus		Dorries (1980)	
Hepatitis A			Locarnini (1979)
Herpes simplex	Falaky (1977)	Kalimo (1977)	Jordan (1981) Kimmel (1982) Morinet (1982)
Influenza A			Burlington (1983)
Mumps	Brown (1970)		Nicolai-Sholten (1980) Ukkonen (1980,81) Ziegelmaier (1981) Meurman (1982)
Papova		Zapata (1983)	Burgiuerre (1980)
Parainfluenza			Ertl (1979) Ukkonen (1980)
Poliovirus		Dorries (1980)	
Rotavirus			Yolken (1978)
Rubella	Cohen (1968) Iwakata (1972) Forghani (1973)	Meurman (1977,78) Kangro (1978)	Voller (1975) Vejtorp (1978,79) Ziegelmaier (1981) Fortier (1982)
Tick borne encephalitis		Frisch-Niggemeyer (1982)	Hofman (1979)
Varicella zoster			Hacham (1980)

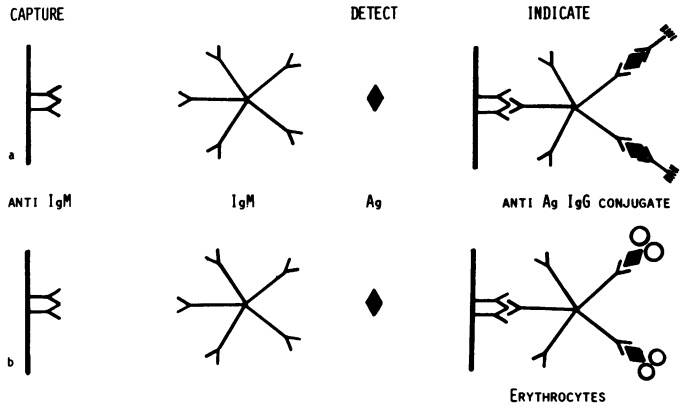

FIG. 8. Solid-phase IgM assay employing capture antibody.

ability to hemagglutinate, erythrocytes can be used as indicators. Table 7 summarizes the various capture antibody systems that have been described [44–61]. A majority of the papers have appeared since 1978, and most are in the area of rubella serology. Tests for hepatitis A and rubella IgM have found their way into routine use due to commercial efforts. Figure 9 shows a modification of the capture antibody method employing an enzyme-labeled antigen [62–67]. The technique has been described for CMV, EBV, VZV, and HSV (Table 8) and appears to have the advantages of simplicity as well as high levels of sensitivity and specificity. Another

TABLE 7
Publications on Solid-Phase Capture Antibody IgM Assays

Virus	SPIT	RIA	EIA
California encephalitis			Jamnback (1982)
Coxsackie B			El-Hagrassy (1980)
Cytomegalo-virus			Yolken (1981)
Hepatitis A		Flehmig (1978)	Duermeyer (1978,79)
Hepatitis B core		Chau (1983)	Moller (1979) Gerlich (1979) Perrillo (1983) Roggendorf (1981,83)
Hepatitis B delta		Smedile (1982)	
Japanese B encephalitis		Burke (1982)	Burke (1982,82)
Mumps	van der Logt (1982)		
Parainfluenza	van der Logt (1982)		
Rubella	Krech (1979) Denoyel (1981) Braun (1981) van der Logt (1981)	Mortimer (1981)	Diment (1981) Isaac (1982) Vejtorp (1981)
Tick Borne encephalitis			Roggendorf (1981) Heinz (1981)

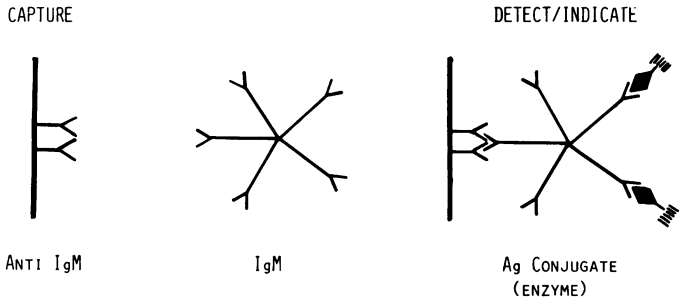

FIG. 9. Antibody capture IgM assay employing enzyme-labeled antigen.

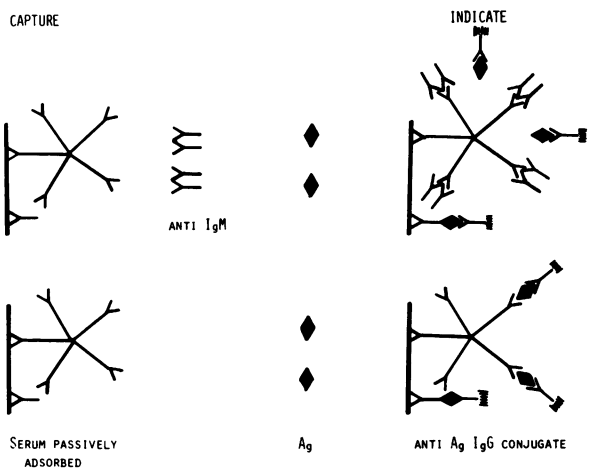

FIG. 10. Solid-phase competitive antibody blocking IgM assay.

approach that has been described is shown in Fig. 10. This competitive antibody blocking test passively adsorbs the test serum to the solid phase then blocks reactive sites in one of the wells before adding antigen and indicator. Differences are then indicative of IgM presence or absence.

Each system mentioned has its inherent problems and advantages [68–73]. Table 9 summarizes the approaches that are required in the two systems to avoid false positive or negative results.

The best example of the use of solid-phase immunoassays employing systems for the detection of viral antigens and antibodies is that for viral hepatitis and is il-

TABLE 8
Publications on Solid-Phase Capture Antibody IgM Assays Using Enzyme-Labeled Detector Antigen

CYTOMEGALOVIRUS	SCHMITZ (1980) KRECH (1982) VAN LOON (1981)
EPSTEIN BARR VIRUS	SCHMITZ (1982)
HERPES SIMPLEX VIRUS	VAN LOON (1981)
VARICELLA ZOSTER	SUNDQVIST (1982)

TABLE 9
Approaches to Eliminate Non-Specific Reactions to Solid-Phase IgM Assays

Assay	Approaches
Capture antigen	1) Treat serum with staphylococcal protein A or anti IgG antiserum to remove IgG.
	2) Remove rheumatoid factor from serum by IgG coated latex, heat aggregated IgG, etc.
	3) Use Fab fragment conjugates.
Capture antibody	1) Use several dilutions to detect interference by endogenous IgM.
	2) Use Fab fragment conjugates.
	3) Certain animal species better than others for detector reagents.

lustrated in Fig. 11. A single serum collected during the acute phase of illness can be tested for hepatitis B surface antigen (HBsAg) and HAV IgM. The presence of either of these markers thus provides a diagnosis within a day. The presence of core antibody (anti-HBc) and absence of anti-HBs (antibody to surface antigen) may mean recent infection with HBV, and a second serum should be requested or a test performed on the first serum for anti-HBc IgM. By the process of elimination of HBV, HAV, CMV, and EBV the patient may be diagnosed as having non-A, non-B hepatitis. Assays for detection of markers of non-A, non-B may soon become available [74]. Using the tests illustrated in Fig. 11 we have had many occasions to perform "stat" testing on health care workers' and patients' sera involved in a needlestick accident and to provide recommendations for the appropriate use of hepatitis B immune globulin (HBIG). Similar testing has identified HBsAg mothers and recommendations for the use of HBIG and vaccine for their babies. Identification of HAV cases have enabled appropriate immunization of their close contacts with immune serum globulin.

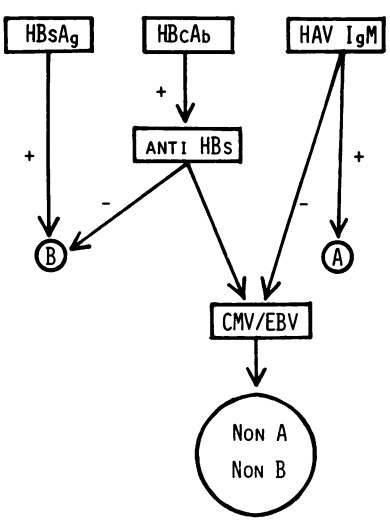

FIG. 11. Rapid testing for viral hepatitis.

TABLE 10
Direct Examination of Clinical Specimens by Electron Microscopy

FLUID	GASTROENTERITIS, CONGENITAL INFECTION, SKIN ERUPTIONS, MENINGITIS, PHARYNGITIS
TISSUE	ENCEPHALITIS, WARTS, LUNG, KIDNEY

DETECTION OF VIRAL PARTICLES

Electron microscopy (EM) techniques are most applicable for the investigation of infections when virus may be present in specimens in concentrations of at least 10^7 particles per ml [75]. Specimens such as feces, vesicle fluid, brain tissue, wart tissue, urine, or serum can be negatively stained with minimum preparation to yield positive results.

Diseases for which EM can play a role in rapid diagnosis include: gastroenteritis, herpes simplex infections, varicella zoster, variola, vaccinia, pustular contagious dermatitis, molluscum contagiosum, warts, and congenital cytomegalovirus (Table 10).

Rotaviruses (Fig. 12), adenoviruses, picornaviruses, astroviruses, caliciviruses, coronaviruses, and Norwalk agents have been viewed in feces from patients with gastroenteritis [76]. We use the technique on a daily basis to diagnose hospitalized patients upon admission for purposes of isolation and reduced nosocomial spread.

Patients presenting with vesicular lesions (ex- or enanthematous) may yield herpes simplex, varicella (Fig. 13), or vaccinia viruses in vesicle fluid. The EM morphology of the herpes viruses allows identification to group, and other laboratory techniques are needed for typing. EM can be used to detect herpes virus particles in brain biopsy material from a patient with encephalitis (Fig. 14), although EM has not been as sensitive as FA (see above). Human papillomavirus (common warts), Orf virus, and molluscum contagiosum pox virus can be viewed in homogenates of solid biopsy tissue.

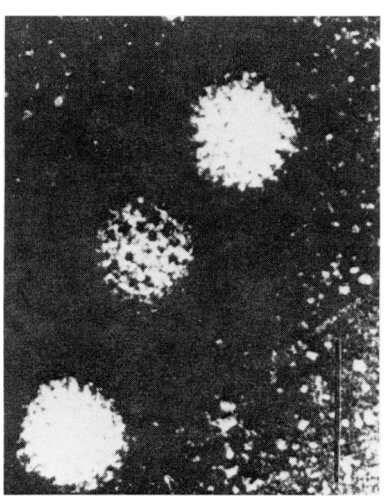

FIG. 12. Rotavirus particles in feces from a patient with gastroenteritis. PTA. Bar represents 100 nm.

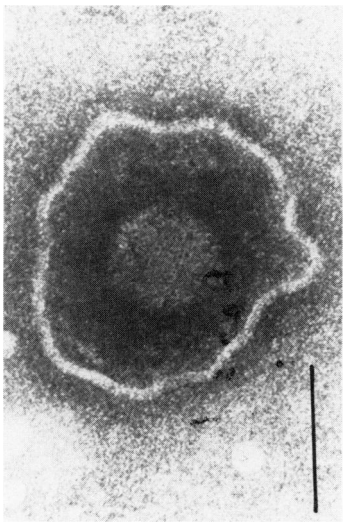

FIG. 13. Varicella zoster virus particle in vesicle fluid from a patient with chickenpox. PTA. Bar represents 100 nm.

Cytomegalovirus (Fig. 15) is usually present in high concentration in the urine of congenitally infected infants [77] but may require some form of enhancement [78].

The most appropriate laboratory technique for the preparation of clinical specimens is negative staining. Thin sectioning techniques have limited applicability to rapid diagnosis. However, a rapid embedding method that takes only two hours has been described [79] and thin sectioning is useful where speed of diagnosis is not important.

The basic requirements for negative staining have been described in detail by Almeida [80]. The most commonly used stain is phosphotungstic acid (PTA) as a 2–4 percent solution adjusted to a pH of 6 to 8, with 1 N potassium hydroxide, and stored as a working solution at 4°C. Formvar-carbon coated 400 mesh copper grids provide the most versatile characteristics for specimen viewing. A disposal container of hypochlorite or similar solution should be used for discarding contaminated materials and a flame present for decontamination of forceps.

Fluid specimens are centrifuged for one hour at 15,000 *g* with resuspension of the pellet in a small amount of distilled water before staining [81]. A more rapid and simpler technique involves placing a drop of the specimen on a drop of sterile distilled water sitting on a waxed surface (Fig. 16). A grid held by fine forceps is touched

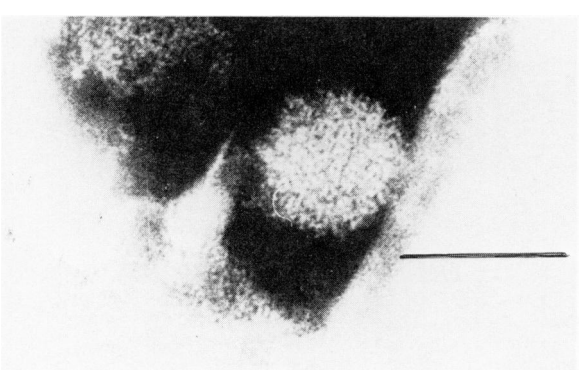

FIG. 14. Herpes simplex virus nucleocapsid in brain tissue. PTA. Bar represents 100 nm.

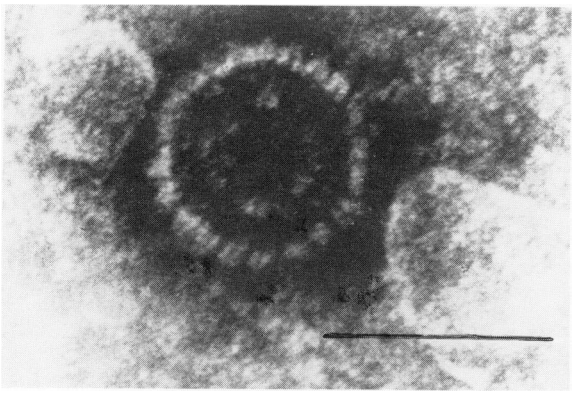

FIG. 15. Cytomegalovius in urine from a congenitally infected infant. PTA. Bar represents 100 nm.

to the drop, held upright, and stained with a drop of PTA. Excess fluid is removed with a torn strip of filter paper, after which the specimen is dried before examining in an EM. The total process takes about five minutes. Application of centrifugation is helpful in making a preparation of better quality and often depends on the type of clinical specimen submitted. Feces can be prepared by making a 10–20 percent suspension in distilled water. Clarification in a bench centrifuge may be necessary for some suspensions; however, rotaviruses are usually easily seen without centrifugation.

Vesicle fluid should be collected from unbroken lesions using a tuberculin syringe containing a small amount of distilled water. A sheath should be placed over the needle, and tape applied to the plunger and sheath; then the syringe should be transported to the laboratory inside an appropriate container. Urine which is cloudy should be clarified by centrifugation at 2,500 *g* for 30 minutes. The supernatant fluid will usually yield virus more readily if as large a volume as possible is centrifuged for one hour at 15,000 *g* with staining of the resuspended pellet. Techniques of enhancement have proven useful for urine specimens. Serum contains many low molecular weight proteins which need to be washed out by diluting with an equal volume of distilled water. The centrifugation step is necessary and may require recentrifugation to enable a clean specimen.

Biopsy or autopsy tissue is cut into small (1 mm) cubes and placed on a metal planchet, which enables several cycles of freezing and thawing. An alternate method involves mechanical homogenization using a mortar and pestle or homogenizer. Following this, a relatively smooth suspension can be achieved by mixing with small amounts of distilled water using a fine-bore pasteur pipette. Best results are then achieved by differential centrifugation before staining with PTA.

Conjunctival scrapings usually contain small amounts of tissue. CSF will seldom

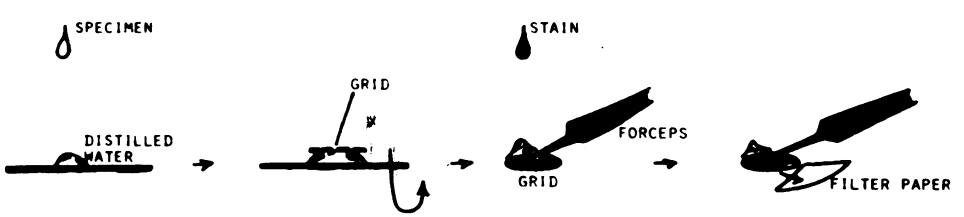

FIG. 16. Negative staining procedure for electron microscopy.

TABLE 11
Electron Microscopy Visualization
Enhancement Techniques

1. **Pseudoreplication**
2. **Agar Gel Diffusion**
3. **Ultracentrifugation**
4. **Immune Electron Microscopy**

yield a virus [82]. Both of these specimens should be processed by the rapid staining technique. Sputum specimens should be diluted in saline and then homogenized or treated with 20 percent n-acetyl cystein. Differential centrifugation or some form of enhancement is usually necessary to concentrate the specimen. If concentrations of viruses are lower in these specimens or others, techniques to enhance visualization are necessary (Table 11). Both pseudoreplication [83] and gel diffusion [84] concentrate the virus particles by allowing the fluid phase to pass through agar. Using ultracentrifugation techniques, both influenza A and parainfluenza 3 viruses were seen in throat washings from patients (Figs. 17 and 18). Using solid phase immune electron microscopy techniques [85] we were able to concentrate BK virus 100- to 1,000-fold (Fig. 19). Similarly, by coating SPA treated grids with rabbit antiserum to CMV, the method was able to detect virus in urine from CMV-infected kidney allograft patients (Fig. 20).

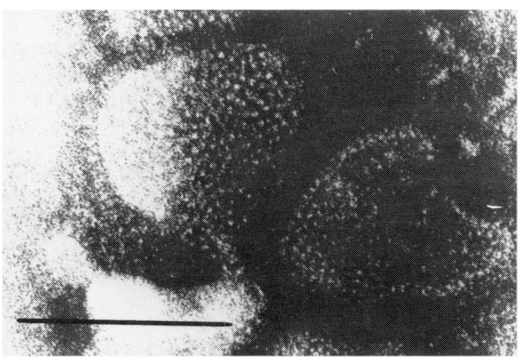

FIG. 17. Influenza A virus particles in throat washings following ultracentrifugation. PTA.

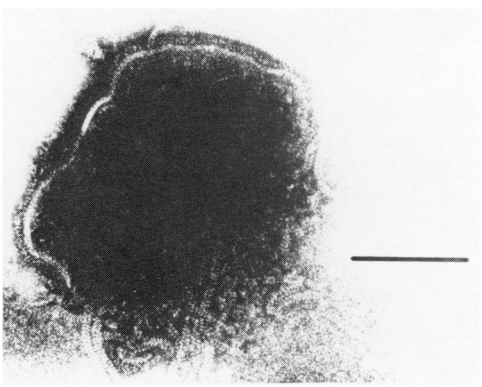

FIG. 18. Parainfluenza type 3 virus particles in throat washings following ultracentrifugation on an airfuge. PTA. Bar represents 100 nm.

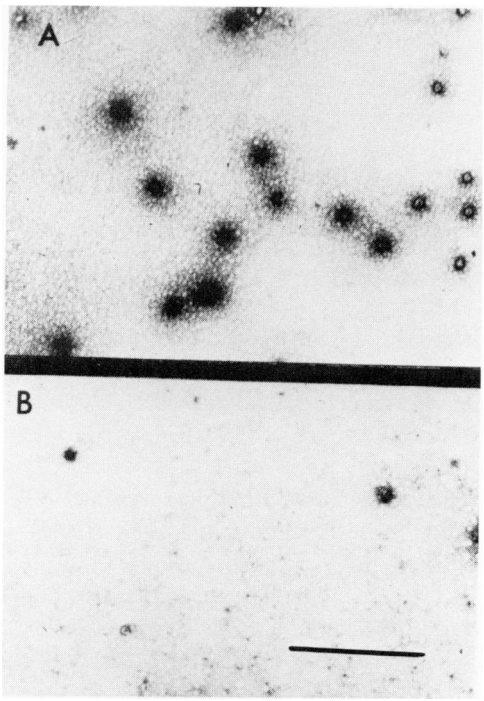

FIG. 19. Solid phase immune electron microscopy preparation of BK virus. **A** Antibody-treated grid; **B** Non-treated grid. Uranyl acetate. Bar represents 1,000 nm.

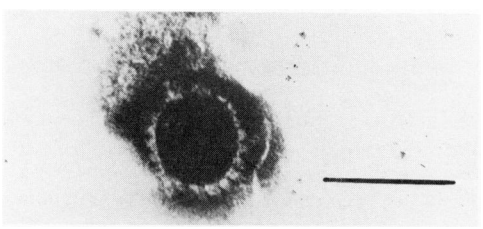

FIG. 20. Solid-phase immune electron microscopy preparation of cytomegalovirus in urine. Grid was treated with staphylococcal protein A and anti-CMV antibody. Uranyl acetate. Bar represents 100 nm.

COMMENT

Table 12 lists the various techniques employed in rapid viral diagnosis. More than one approach may be necessary to uncover a viral etiology in a particular patient. Knowledge of test availability coupled with clinical information should lead to a diagnosis in sufficient time to influence patient and/or population management or treatment.

TABLE 12
Rapid Viral Diagnostic Techniques

1. Culture
2. Microscopy
3. Detection of antigens in clinical specimens
4. Detection of early antibody responses
5. Detection of nucleic acids or enzymes

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