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HANDBOOK OF CLINICAL NEUROLOGY

P. J. VINKEN and G. W. BRUYN

INFECTIONS OF THE NERVOUS SYSTEM

PART I

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PART I

Edited by

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Foreword to volumes 33, 34 and 35

The contents of these three volumes are fairly well defined by the title 'Infections of the Nervous System'. The contents of each volume are further defined by the decision to dedicate each volume to a separate class of etiologic agents. The further organization of each volume then posed its own particular questions.

The first volume was limited to infections caused by bacterial agents. The major issue to be decided was whether to organize this volume by etiologic agent or by type of infectious process. Other problems included which bacterial toxins to include and how much emphasis should be placed on the therapeutic aspects of each disease. After much discussion among the editors and many colleagues, especially Dr. Stuart Levin, it was decided to organize the volume primarily along etiological lines but to include separate chapters on specific types of infections which can be caused by numerous bacterial agents but in which the clinical characteristics of the syndrome are more dependent on the location of the infection than the causative agent. The chapters on brain abscesses and focal suppurative infections is an example of this approach. Bacterial meningitis is, of course, the most important class of such infections and is represented by both a general introductory chapter and a group of chapters on specific etiologic agents.

The decision to include a chapter on chronic arachnoiditis was not based on purely etiologic consideration but on the clinical consideration that this syndrome at times must be differentiated from bacterial infections of the linings of the brain and spinal cord.

Each year new antibiotics appear and the spectrum of bacterial responses to older antibiotics changes. Because of these two factors, up-to-date considerations on the pharmacologic therapy of bacterial infections can quickly become outdated and, it might be argued, should not be included in a Handbook of this nature. The fact remains, however, that we can medically treat many diseases but can actually cure only a few and of these most are infectious. To deemphasize the most up-to-date pharmacologic approaches to these potentially curable but life threatening diseases could well be considered unjustified. We believe that despite the built in obsolescence, modern chemotherapy must be given its just due and major attempts have been made to ensure that the therapeutic aspects (both medical and pharmacologic, and, where applicable, surgical) are thoroughly and accurately presented.

Concerning bacterial toxins, those toxins which are the products of active infections within the body, e.g., diphtheria toxin and tetanus toxin, were included while bacterial toxins in which there is no actual infection, such as botulism, will be included in the volume on toxic agents.

The second volume is limited to viral and rickettsial diseases. It also includes a series of chapters on diseases of unknown etiology in which viruses or viral-like agents may play a role. Once again this volume includes both introductory general chapters as well as more specific chapters on particular etiologic agents. This field is one of great excitement including the work on slow virus infection which resulted in a Noble Prize in 1976 for Carleton A. Gadjusek and perhaps even greater potential as the complex relationship between immunology and virology becomes better understood. Professor Richard Johnson, whose advice on the organization of this volume was most helpful, pointed out that it is often unclear where the field of virology ends and the field of immunology begins. Because of this a separate chapter on the immunologic aspects of viral infection has been included. This serves as an introduction to specific chapters on viral-induced syndromes with immunologic aspects and on the relationship of viruses to multiple sclerosis.

Many inflammatory and presumably infections diseases of unknowm etiology have been included in this volume. These include such topics as Behçet's disease, acute cerebellar ataxia, opsoclonus, Bannwarth's syndrome, acute hemorrhagic leukoencephalitis and chronic benign lymphocytic meningitis. The logic of including all of these chapters can, we are sure, be challenged since it is quite likely that neither viruses nor viral related immunologic processes will finally be implicated in all of these disorders. Since in each case, one of these mechanisms remains a strong possibility, the discussion was made to include all of these disorders in this volume. Special recognition should be given to Dr. Robert M. McKendall for his help in organizing this volume.

The third and last volume includes diseases caused by all other classes of infectious organisms. In many ways this was the easiest of all the three volumes to organize since it is arranged entirely by etiologic agents. The complexity comes from the vast array of protozoa, helminths, and mycotic agents which are able to cause disease in man. Professor J. O. Trelles gave us valuable advice on the organization of this volume for which we remain indebted.

As always we are especially indebted to the editorial staff, in particular Brenda Vollers and Robert Stanley for their careful and thoughtful work which has helped to keep editorial delays and errors to an absolute minimum. We also recognize the contributions of Ms. Pat Gerdes and Ms. Genevieve Logan whose organization of the editorial work in Chicago was a major factor in the production of these volumes.

P. J. V.
G. W. B.
H. L. K.

Acknowledgement

Several illustrations and diagrams in this volume have been obtained from other publications. Some of the original figures have been slightly modified. In all cases reference is made to the original publications in the figure caption. The full sources can be found in the reference lists at the end of each chapter. The permission for the reproduction of this material is gratefully acknowledged.

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Contents

CHAPTER 1

Bacterial meningitis

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History

Bacterial meningitis must have been a scourge of mankind through the millennia. Descriptive terms date to Hippocrates who referred to 'water on the brain'. Medical history is replete with embellishing labels such as phrenitis and dropsy of the brain, but these early descriptions reveal little etiologic information. An epidemic of meningococcal disease was described in 1806 but the agent was not identified and cases were interpreted as possible unusual manifestations of the commonly known infectious diseases. A major breakthrough occurred in 1887 when Weichselbaum described Neisseria meningitidis as the etiological agent of epidemic meningitis and in 1899 Slawyk established the significance of H. influenzae. Quincke introduced the diagnostic lumbar puncture in 1891, quantitating manometric pressure, specific gravity and total protein. Shortly thereafter Widel had investigated the cytology, Plant the serology, and Mastrezet the chemical composition of CSF (Merritt and Fremont-Smith 1938). At the turn of the century, the classic abnormalities of these parameters as seen in bacterial meningitis were well known but the inability to distinguish the pathogen was acknowledged. These measurements, together with immunological and bacteriological attempts to specifically identify the bacterial agent remain the mainstay of diagnosis in bacterial meningitis. The coming of the therapeutic era emphasized the importance of diagnosis. The course of an acute illness which, untreated, had a 75–100% mortality, could now be substantially altered.

CLINICAL MANIFESTATIONS

There have been a number of excellent reviews on bacterial meningitis published in the last 15 years which have concentrated on the diagnosis and management of this serious disease (Carpenter and Petersdorf 1962; Quaade and Kristensen 1962; Haggerty and Ziai 1963; Swartz and Dodge 1965; Berman and Banker 1966; Hameleton and Davies 1975). The classical physical findings of meningitis can be divided into three groups: fever, neck rigidity and cerebral dysfunction. Fever and chills are secondary to bacterial invasion of the blood stream and spinal fluid, eventually leading to release of leukocytic pyrogen and hypothalamic stimulation. Inflammation of the subarachnoid space activates protective reflexes resulting in nuchal rigidity, hyperextension of the neck and spine, and the traditional Brudzinski and Koernig signs. The Brudzinski sign is more sensitive if neck flexion is attempted with the patient in a sitting position with legs extended parallel to the floor. Cerebral dysfunction is the most consistent abnormality and may manifest itself by nausea,

References, p. 15

vomiting, headache, irritability and excitability or significant depression of mental function. The dysfunction is due to a combination of cerebral edema and unknown toxic effects on the underlying cortical tissue. An analysis of five series of pediatric meningitis (Smith et al. 1973) revealed rash in one-sixth, anorexia in one-fifth, listlessness and irritability in one-third, convulsions in one-third, stiff neck in two-fifths, vomiting in two-thirds and fever in nine-tenths of cases. The frequency of findings is skewed lower by the inclusion of neonates who manifest a lesser frequency of physical signs. Many exanthems, including maculae, petechiae, and ecchymoses are typical but not pathognomonic of meningococcal disease. Herpes simplex labialis is seen in 20–70% of cases of bacterial meningitis; rarely present on admission, it usually appears mid-recovery, and is of no aid in differentiating the bacterial etiology.

EPIDEMIOLOGY

The relative frequencies of the three major causes of bacterial meningitis differ from decade to decade and from country to country. H. influenzae B is the most common cause of meningitis in the United States and Australia while N. meningitidis is most frequent in England and Scandinavia. E. coli, especially those that contain capsular K 1 antigen and Group B streptococci, are the usual pathogens in neonates who additionally are as susceptible to 30–40 other bacteria. Between the ages of two months and five years the incidence of H. influenzae B is greatest, followed by N. meningitidis, and then S. pneumoniae. The latter is most common after 30–40 years of age while N. meningitidis is the prevalent species in the interim. Recently, the frequency of H. influenzae meningitis in adults is increasing (Norden et al. 1970). Theoretically this may relate to the overuse of broad spectrum antibiotics in children leading to decreased subclinical carriage of H. influenzae or E. coli possessing K 1 antigen. Antibodies to both may react with H. influenzae capsular antigen (Dackos and Weinstein 1951; Weinstein 1970) and hence the protective level may be diminished. Indeed, while more than 90% of adults in the 1930's had H. influenzae neutralizing antibodies, their prevalence has now decreased to 30–50% (Norden 1974; Norden et al. 1970). We should anticipate a further rise in adult H. influenzae meningitis. N. meningitidis has not changed its age distribution but varies serotypically. In the early 1900's Type A predominated in the U.S. In the 1950's, related to sulfa resistance, Type B became most frequent and was soon superseded by Type C. In areas where Type C vaccine is used, Type Y is the emerging meningococcus. Unlike the meningococcus, both H. influenzae B and S. pneumoniae meningitis are directly related to race and economy, an increased incidence being seen in blacks and lower socioeconomic groups (Parke et al. 1972; Frazer et al. 1973). Within a given social stratum, blacks remain more susceptible and sickle cell disease carries an increased risk within the black population.

Antibiotic usage, vaccines, the improved prognosis of many previously fatal diseases, immunosuppressive therapy, host and iatrogenic factors have led to a changing spectrum of etiologic agents in bacterial meningitis. Fifty percent of infections seen in modern hospitals are hospital acquired, and hospital acquired bacterial meningitis is increasing. This is rarely due to the common bacterial pathogens (Hodges and Perkins 1975). Predisposing factors in hospital acquired meningitis include surgery of the neuraxis, surgery of contiguous or distant sites, and infections in other sites of the body. Most of the patients acquiring this infection are receiving antibiotics at the time.

Meningitis has been associated with chronic non-infectious diseases and knowledge of the underlying illness can suggest an etiologic agent. Gram-negative rod meningitis is increasingly found, particularly in the elderly with underlying disease and recent surgery (Frazer et al. 1973). Narcotic addicts seem predisposed to coagulase positive Staphylococcus aureus or Pseudomonas aeruginosa meningitis, usually associated with endocarditis.

Neoplastic diseases have had unique associations with specific infectious agents (Chernik et al. 1973). Head and neck cancer, without immunosuppression, predisposes to coagulase posi-

References, p. 15

tive staphylococcal meningitis and less commonly to E. coli and P. aeruginosa. Listeria monocytogenes is the single most common cause of acute meningitis in patients with lymphoma and leukemia although S. pneumoniae and P. aeruginosa are also important (Gantz et al. 1975). Nocardia asteroides (a bacterium often called a fungus) is a rare, but very difficult to treat, cause of meningitis in patients with leukemia and lymphoma and is often associated with brain abscesses. While bacteria are responsible for 95% of non-viral infections of the CNS in an outpatient population, fungi and protozoa make up one-third of these infections occurring in patients receiving steroids and immunosuppressive therapy for malignancy or prevention of transplant rejection. Cryptococcus neoformans is the most common fungus and presents as subacute or chronic meningitis. Toxoplasma gondii and the herpes viruses are less common but important CNS pathogens. These illnesses may be considered complications of medical progress.

Infection brought about by foreign bodies, e.g. catheters or shunts used to treat hydrocephalus, has been the best evaluated of the previously noted diseases of medical progress. Infection rates have ranged from 3–20% and as with infected heart and hip prostheses, the coagulase negative staphylococcus is the predominant pathogen (Schimke et al. 1961). Diptheroids are the other low grade pathogens frequently involved, while skin flora and the major meningitis pathogens occur rarely. These organisms are often considered 'contaminants' and the physician must be wary of their presence in blood or spinal fluid. Cultures of lumbar or ventricular fluid are positive in one-half to two-third of cases and multiple cultures are usually necessary to confirm their significance. A false sense of security may exist because clinical signs of infection are often lacking for prolonged periods of time, and the temperature and white blood cell count may be normal. Tricuspid endocarditis, hypocomplementemic glomerulonephritis and multiple bland or septic pulmonary emboli (Emery and Hilton 1961; Schoenbaum et al. 1975) may complicate ventriculo-atrial shunts and are related to the persistent intravascular infection. Ventriculoperitoneal and ventriculopleural shunts have the same rate of CNS infection as the ventriculo-atrial shunt. However, bacteremia is rare, while inflammation of the subcutaneous tissue and/or pleuroperitoneal spaces may be obvious.

Skull fracture leads to a high risk of bacterial meningitis (Hand and Sanford 1970). In open fractures many organisms can and do cause meningitis. Antibiotic prophylaxis is unlikely to be successful and immediate surgical closure is usually indicated. When closed skull fracture is associated with leakage of spinal fluid into the middle ear, sinuses or nares the situation is more complicated. S. pneumoniae is the most frequent pathogen, but other etiologies occur and are unpredictable. Studies of sulfa and penicillin prophylaxis immediately post trauma have yielded conflicting results (Leech and Paterson 1973). Prophylactic antibiotics are probably unwarranted but careful observation and early therapy for meningitis are mandatory (Ignelzi and Van der Ark 1975). The spinal fluid leak may be subclinical and require the use of isotope cisternography (DiChiro et al. 1968; Lancet editorial 1972) for its demonstration. Indeed there may be no history of skull trauma. Recurrent pneumococcal meningitis is a statistically unlikely event and dictates a search for CSF rhinorrhea. If a post-traumatic leak fails to close in 1–2 months, or if a leak is detected after recurrent meningitis, surgical closure is recommended. In the authors' opinion, lifelong low dose sulfa or penicillin prophylaxis should be administered to those patients with unclosed leaks. This regimen is likely to suppress or eradicate the pneumococcus without disrupting the character or antibiotic sensitivities of the remaining resident flora.

Recurrent meningitis due to E. coli, S. epidermidis, diphtheroids or pseudomonas may be seen in patients with congenital dermal sinuses. These may occur anywhere from the vertex to the coccyx and are usually midline. They are most frequently identified as dimples in the occipital or lumbosacral regions. The sinus may be marked by several long hairs in an otherwise hairless area, or shaving may be necessary before its discovery. Complete surgical extirpation is necessary to prevent recurrent meningitis with these difficult to treat bacteria (Matson and Jerva 1966).

The risk of bacterial meningitis is minimal

References, p. 15

even in the presence of nasopharyngeal carriage of the common pathogens. A carrier of the meningococcus develops bacterial meningitis 1 in 1,000 to 1 in 10,000 times (Artenstein 1975). Assuming a 20–40% carrier rate in the general population, pneumococcal meningitis will develop 1 in 10,000 to 1 in 50,000 times. From a 30% carriage rate of H. influenzae B in children 1–5 years old and the occurrence of 100 cases of meningitis per 100,000 children, the carriage risk of 1 in 300 is calculated (Parke et al. 1972; Robbins et al. 1973).

The calvarium is external to the successive layers of epidural space, dura (periosteum), subdural space, arachnoid, subarachnoid space (spinal fluid layer) and the pia (visceral covering of the brain). However, the subarachnoid space is the only continuous cavity, and envelopes, but is non-adherent to, the convexities and concavities of the brain and spinal cord. The response to bacterial infection in the subarachnoid space is exudation of white blood cells and fibrin. Only on rare occasions will the organism or inflammatory response extend through the surrounding membranes. Bacteria may directly enter the subarachnoid space via the bloodstream, ears and sinuses, traumatic or congenital defects, instrumentation, retrograde venous flow and the paravertebral lymphatic plexus. Additionally, hematogenous spread may result in parenchymal granulomas or abscesses which eventually rupture into the ventricular or subarachnoid space (Harter and Petersdorf 1960).

In the majority of patients with meningococcus, H. influenzae or pneumococcal meningitis bacterial entry is a complicated process. Colonization of the nasopharynx is followed by invasion of the submucosal lymphatics and bacteremia follows. Rarely the bacteria will enter the subarachnoid space by way of the meningeal vessels and choroid plexus. Experimentation with H. influenzae in rats has shown the dural sinuses to be invaded secondary to bacteremia with subsequent direct extension through the pia arachnoid (Moson et al. 1974). Experimental bacteremia, following cisternal or lumbar puncture, will consistently incite meningitis at the point of entry (Petersdorf and Luttrell 1962; Petersdorf et al. 1962).

Although poorly understood, the blood-brain barrier is quite effective in adults where 99% of bacteremic patients will not develop meningitis. However, in neonates one-third of those with bacteremia develop meningitis. Animal inoculation of bacteria into the subarachnoid space results in bacteremia in one-third. Human patients with recurrent meningitis due to anatomical defects, the naturally occurring equivalent of experimental inoculation, will have an associated bacteremia in 30–50% of the time. Therefore, as is demonstrable with trypan blue dye, the blood-brain barrier appears to function unidirectionally.

An axiom of infectious disease relates clinical disease to an interplay of host and organism, and meningitis should be no exception. While speculative, the capacity to cause meningitis may be related to bacterial receptor sites, adhesiveness, invasiveness or virulence. Viral infections have been considered potential triggers of meningitis through suppression of white cell function and subsequent local invasion of the nasopharyngeal flora (Leedom et al. 1965). Studies of meningitis patterns as they relate to blood group and tissue typing have not revealed a consistent pattern (Robbins et al. 1973). The role of mucosal IgA is uncertain, while serum-neutralizing antibodies are effective in preventing septicemia and meningitis (Artenstein 1975) in the absence of a direct communication to the subarachnoid space. Neutralizing antibodies are not present in the index case but household contacts will have high titers stimulated by prolonged subclinical carriage. The gram-negative enteric flora, and specifically E. coli K 1 capsular antigen, may stimulate cross-reactive antibodies (Leedom et al. 1965). These 'natural antibodies' may occur in high protective titers or allow an anamnestic rather than primary immune response.

DIAGNOSIS

Examination of cerebrospinal fluid

The development of non-invasive techniques in the evaluation of disease of the CNS have not supplanted lumbar puncture as the sine qua non of bacterial meningitis (Petito and Plum 1974). Clinical suspicion must provide the stimulus to consider lumbar puncture, and one must then

References, p. 15

weigh the octageneric issue-indication vs. contraindication (Editorial Brit. Med. Journal 1975). Tetracycline, hypervitaminosis A, upper lobe pneumonia, cervical adenitis, tonsillitis, shigellosis, typhoid, scarlet fever and other non-CNS infections can produce nuchal rigidity and/or a bulging fontanel. The mortality rate of 75–100% in untreated bacterial meningitis dictates the performance of a lumbar puncture, despite these alternate diagnoses. A normal spinal tap in a patient with clinically suspect meningitis is never cause for apology. Lumbar puncture led to a diagnosis of bacterial meningitis in 3.3% of all taps done in an academic pediatric emergency room (Smith et al. 1973).

Febrile seizures occur in 2% of patients under two years of age without evidence of CNS infection, and are indications for diagnostic lumbar puncture unless a past history of recurrent febrile seizures is obtained (Samson et al. 1969). A series of 152 cases of bacterial meningitis revealed 27 with fever and seizures, and 11 of these (all between one and 16 months of age) had no other signs of meningitis (Menkes 1973). Compiling the risk of febrile convulsions and the risk of a combination of seizures and fever without meningeal signs, yields an estimate of one case of bacterial meningitis per 300 febrile seizures.

In the absence of organic obstruction of the subarachnoid space, a lumbar puncture is representative but not identical to fluid obtained at a higher level. Comparison of lumbar to cisternal fluid reveals a higher cell count, percentage of polymorphonuclear forms and protein at the lumbar site. The sugar, on the other hand, is lower.

For practical purposes the diagnosis of bacterial meningitis is made when the lumbar puncture reveals purulent fluid with a white cell count greater than 1,000 cells/μl, the majority of which are polymorphonuclear forms. A positive bacterial gram stain and/or a low sugar increases the confidence of the decision to treatment. Repeated lumbar puncture is rarely necessary (Wehrle 1973) except for three well-defined circumstances.

– (1) The initial lumbar puncture is not diagnostic: (a) Eastern equine encephalitis (EEE) often shows a white cell count as high as 2,000 cells with a predominance of polymorphonuclear forms, and a conversion to lymphocytes requires days. The change to lymphocytes with a repeated tap is unlikely to occur even after several days. By current criteria these patients with EEE should be appropriately treated for bacterial meningitis. Contrariwise many patients with viral infections of the CNS have white cell counts of less than 1,000 cells but with a predominance of polymorphonuclear pleocytosis, enterovirus and St. Louis encephalitis viruses being exemplative. Early bacterial meningitis may also have only a few dozen to a few hundred cells, a normal sugar and will exactly mimick an aseptic process. If no antibiotics are given, repeated lumbar puncture within 2–12 hours will usually distinguish between viral and bacterial meningitis (Feigin and Shackelford 1973). The spinal fluid of bacterial meningitis will become more purulent while that of viral meningitis remains stable or changes to a predominance of lymphocytes. Although the potential danger of proven bacteremia at the time of the negative tap generates controversy, a repeated lumbar puncture will solve more diagnostic dilemmas than it will create (Moore and Ross 1973; Rapkin 1974; Fischer et al. 1975). The less than 10% of patients in whom a diagnosis remains unclear will be treated again or re-tapped on the basis of clinical judgement.

(b) The rare syndrome of non-infectious purulent meningitis following neurosurgery manifests all the signs, symptoms and traditional spinal fluid findings of bacterial meningitis. Additionally, often many red blood cells are present. The protein and white cell count may exceed 200 mg% and 2,000 per cu mm, respectively. A low sugar is common and persists for days. The meningitis occurs within 48 hours of surgery, most frequently after posterior fossa procedures, and is not tumor dependent. A delayed syndrome has occurred weeks postoperatively. A review of 35 cases (Carmel et al. 1974) constituting 70% posterior fossa surgery, revealed only one case of bacterial meningitis. Careful gram stain and culture techniques will usually resolve the problem. Immunologic studies have not been reported. If the gram stain is negative, and the patient is stable, antibiotics should be withheld and serial lumbar punctures performed. Antibiotics are of no benefit

References, p. 15

in the non-infectious cases. Steroids may improve signs, symptoms and spinal fluid findings and prevent subsequent obstructive complications. The rare occurrence of a bacterial meningitis demands bacteriologic identification because, as with posttraumatic purulent meningitis, a wide range of bacteria including anaerobes, may be etiologic.

– (2) The initial lumbar puncture is diagnostic: when the etiology of the meningitis is one of the major bacterial pathogens and if appropriate therapy is being given, retapping will rarely be indicated. Failure to clinically improve, and persisting fever, are the major clinical parameters dictating repeated tap. A second puncture should also be considered if the organism is unusual, the antibiotic unproven, or bacteriologic and sensitivity studies are confusing.

– (3) The initial lumbar puncture is diagnostic and an adequate course of appropriate therapy is given: in this setting lumbar puncture is usually performed to verify that vague symptoms and fever (perhaps related to the recent antibiotic) are not due to relapsing meningitis. Normal spinal fluid results should not be used as an indication to terminate therapy prior to the recommended duration. Length of therapy has been determined on the predictability of relapse and hence a short course may be the harbinger of doom.

Thus, lumbar puncture plays a role during four states of bacterial meningitis – initial diagnosis, diagnostic confusion, clinical atypia, and, most infrequently, after a satisfactorily completed clinical therapeutic course.

Contraindications. Raised intracranial pressure secondary to localized pathology, rather than from diffuse meningitis, is the single absolute contraindication to a lumbar puncture. Intracranial as well as epidural and subdural masses are usually involved. A history of symptoms, if elicitable, and clinical findings may suggest such a lesion. A history extending over weeks to months is incompatible with acute bacterial meningitis. However, headaches, progressive mental deterioration and meningeal symptoms of less than three days duration do not exclude a space-occupying lesion. Papilledema is rarely seen in acute bacterial meningitis and warrants caution. Skull X-rays revealing displacement of a calcified pineal and/or erosion of the posterior clinoids indicate a mass effect. When a posterior fossa lesion is suspected, arteriography or EMI scanning should be performed prior to lumbar puncture. Reye's syndrome and lead poisoning are non-space-occupying lesions where post puncture neurologic deterioration is a probable (Beyers 1973) contraindication. Asymmetrically increased spinal fluid pressure may cause herniation of the uncus subtentorially, of the cerebellar tonsils through the foramen magnum, or of the cingulate gyrus subfalcially, and lumbar puncture may precipitate or exaggerate the process. Clinically there will be loss of consciousness, abnormal respiratory patterns, hemiparesis and pupillary dilatation. A review (Duffy 1960) of 30 such catastrophes revealed 50% of the patients deteriorating within minutes and 100% within 12 hours of diagnostic lumbar puncture. Only 10% did not manifest focal findings, papilledema or X-ray changes suggestive of a mass prior to lumbar puncture.

Bleeding diatheses, localized lumbar infection or dermatitis, and cardiopulmonary disease in infants are relative contraindications to lumbar puncture. If acute bacterial meningitis is suspected, the tap can and should be performed. Platelet packs and fresh plasma can be given to correct thrombocytopenia and coagulation factor deficits, respectively. In the presence of hemophilia, Factor VIII concentrate may be administered. The most skilled tapper, using the smallest possible needle, should perform the procedure. When lumbar dermatologic infections are evident, a cisterna magna tap will avoid iatrogenic introduction of bacteria. It is important to recall the variant results when comparing lumbar and cisternal fluid. Lumbar puncture may precipitate cardiopulmonary arrest in infants with chronic diseases of these systems (Margolis and Cook 1973).

Complications of lumbar puncture. Headaches are the most common complication of lumbar puncture. As with herniation, they are due to the pressure column of spinal fluid at the lumbar dural rent rather than to the absolute volume of fluid

References, p. 15

removed. The height of the pressure results in continuous flow and failure to seal the tear. Removal of sufficient fluid to decrease the pressure would theoretically facilitate closure of the defect, but this is unsubstantiated. A single puncture with a small gauge (20–22) needle, followed by assuming the prone position for several hours, will decrease the occurrence of headaches from 35% to 0.5% (Brocker 1958).

A postulated complication of lumbar puncture has been the conversion of bacteremia to bacterial meningitis secondary to arachnoid trauma. Patients with normal spinal fluid early in acute septicemia have later developed meningitis with the same organism (Rapkin 1974; Fischer et al. 1975). This is especially seen in infants. The benefit to risk ratio supports the use of lumbar puncture in bacteremia, but if the patient is a subsequent unexplained therapeutic failure a repeated spinal tap is indicated.

An important, but seldom considered complication of lumbar puncture is the acquisition of false laboratory data and its imminent adverse therapeutic implications. False-positive gram stains have been caused by failure to alcohol cleanse the slide prior to smear, contaminated collection vehicles, lack of millipore filtering and infrequently used gram stain material (Musher and Schell 1973; Weinstein et al. 1975). The use of an open needle can track epidermal tissue and bacteria into the spinal fluid, leading acutely to false-positive gram stains and chronically to epidermoid tumors of the spinal cord. Theoretically an iatrogenic meningitis may ensue. The use of anesthetics or dyes at the time of lumbar puncture may result in bacterial contamination, chemical meningitis or endotoxinlike activity (Rendell 1954; Barnes and Fish 1972). The limulus lysate test has been used to test for endotoxin prior to intrathecal injection (Rhodes et al. 1974).

Identification of etiologic agent. Having performed a lumbar puncture one is concerned with those laboratory data which are of immediate diagnostic therapeutic import. Culture in the untreated patient reveals the pathogen 80–90% of the time but requires a minimum 48-hour delay. Gram stains have a 70–80% positivity, but false-positives and negatives reduce their overall usefulness by one-half. The characteristic purulent appearance and cell counts have been noted. In addition to bacterial meningitis, cell counts greater than 1,000/μl, with predominantly polymorphonuclear forms, may be seen with leukemic infiltration (Schwartz et al. 1975), irradiation, protozoal meningitis (Martinez et al. 1975), tuberculous meningitis, or epidural and subdural abscesses. When parameningeal abscesses occur, lumbar puncture may result in herniation or penetration of the purulent collection. Cytospin is helpful in identifying neoplastic cells, and hanging-drop preparations may detect the protozoan Naegleria or Acanthamoeba. The role of viral infection and chemical irritation in creating diagnostic confusion has been mentioned.

Spinal fluid sugar. The spinal fluid sugar is dependent upon the blood sugar and in a steady state will exceed 50% of the plasma glucose level. One to two hours are required for equilibration after a change in blood sugar, and this lag must be considered when interpreting the results of simultaneously obtained specimens. The eventual level is determined by active shunting, simple diffusion and brain consumption. Consumption increases early in the course of bacterial meningitis. Bacterial utilization is of little relevance to the level and intraventricular injection of pneumococci has resulted in an early increase in spinal fluid sugar. In an untreated patient the association between spinal fluid sugar and cell count is a correlation and not an interdependency. In the presence of bacterial inflammation the brain will consume approximately 75 mg of glucose per minute, while the usual number of polymorphonuclear cells present would require a minimum of one hour to consume this amount.

Hypoglycorrachia – a spinal fluid sugar content less than 40% of a simultaneously obtained blood sugar – is classically associated with bacterial meningitis but is more valuable in differentiating tuberculous from viral meningitis than in differentiating bacterial from aseptic meningitis (Menkes 1969). Meningitis due to herpes simplex, herpes zoster (Wolf 1974), varicella and mumps (Wilfert 1969) has been associated with a low spinal fluid sugar. In this situation the cell count and

References, p. 15