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Septic Thrombophlebitis

(Part 2)

Septic thrombophlebitis is fortunately now an uncommon complication of pyogenic infection although it is being seen with increasing frequency as a very serious sequel of intravenous therapy. In this disorder features of septicemia and septic pulmonary emboli are often superimposed upon the signs and symptoms of local infection and thrombophlebitis. Besides prompt and aggressive treatment of the underlying infection, surgical venous interruption or extraction of infected thrombus is often required for cure.

Dennis G. Maki, M.D.

Since antibiotic therapy was introduced into clinical use septic thrombophlebitis of intracranial veins and dural sinuses, pylephlebitis, and even septic pelvic thrombophlebitis have been encountered less frequently than before antibiotics became available. However, septic thrombophlebitis of peripheral and central veins has become an increasingly frequent complication of intravenous fluid therapy.

The pathophysiology and general clinical features of septic thrombophlebitis were discussed in the first part of this article which appeared in this journal last month. Part 2 of this article covers the clinical and laboratory findings in various types of intracranial septic thrombophlebitis, septic pelvic thrombophlebitis and pylephlebitis, both of which are associated with local infection. Septic thrombophlebitis of the peripheral and the great central veins as a complication of intravenous therapy is then discussed.

Septic Intracranial Thrombophlebitis

The incidence of septic intracranial thrombophlebitis has dropped markedly since the advent of antimicrobial therapy. Brown1 was able to collect only seven cases of septic cavernous sinus thrombosis from 425,000 admissions to the Johns Hopkins Hospital between 1943 and 1960.

Most reported cases of septic intracranial thrombophlebitis have occurred in association with primary bacterial meningitis, suppurrative parame negeal infection, or extracranial infections involving areas such as the paranasal sinuses, middle ear and mastoids, face, or scalp. However, in reviewing the reports of these cases it is often difficult to distinguish true infective intravenous suppuration from bland (aseptic) thrombophlebitis associated with local infection unless the occurrence of bacteremia was noted or histologic examination of thrombus was described. This differentiation certainly has prognostic import. The greatly improved outlook of septic intracranial thrombophlebitis reflects not only the availability of effective antimicrobial agents to treat local infections but probably also earlier recognition of cerebrovenous thrombosis (fostered by superior methods of radiologic diagnosis) and the likelihood that many cases reported as septic intracranial thrombophlebitis are not truly septic.

Cortical thrombophlebitis: Isolated cortical thrombophlebitis, more often bland than septic, is a rare but serious sequel of bacterial meningitis caused by Streptococcus (Diplococcus) pneumoniae, Haemophilus influenzae, or Meningococcus. This condition develops within three to ten days after the onset of meningitis. It may also be a rare complication of suppurrative paranasal sinusitis or other parameningeal suppuration in which case Staphylococcus aureus or anaerobes are the predominant causative organisms.2 Dehydration, which is commonly associated with these infections, may

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1. Brown1
2. Dehydration, which is commonly associated with these infections, may

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SEPTIC CAVERNOUS SINUS THROMBOSIS USUALLY ORIGINATES FROM SUPPURATIVE INFECTION OF ONE OF THREE MAJOR SITES OF DRAINAGE

The "triangle of death": The base includes the upper lip; the apex is located just above the glabellar area of the nose. Extension of infection from this area to the cavernous sinus via the ophthalmic vein is promoted by direct communication via veins which have no valves and a paucity of connective tissue adapted to localization of infection. The pronounced mobility of the skin in the area, because of muscular attachments, likewise interferes with localization and enhances deep spread of infection.

Figure 1.

also contribute to the occurrence of the disease.

Increasing fever is accompanied by neurologic deterioration which is manifested by focal or generalized seizures and focal deficits such as hemiparesis. Cerebrospinal fluid pressure is usually elevated and the fluid may exhibit features of parameningeal inflammation, such as an increased number of mononuclear cells and elevation of the protein concentration; the glucose level is not depressed and microorganisms are not present unless the inciting meningitis has not been appropriately treated or the septic thrombophlebitis arising from extracranial infection has led to a secondary meningitis. Radioisotope brain scans commonly reveal focal areas of increased uptake and electroencephalograms show focal slow waves.²

Septic cavernous sinus thrombosis:¹ ³ ⁴ The cavernous sinuses that parallel both sides of the body of the sphenoid and directly underlie the third, fourth, fifth (divisions I and II), and sixth cranial nerves and sympathetic outflow to the eye, receive extracranial drainage from three sources: 1) the upper face through the superior ophthalmic veins, 2) the sphenoid and posterior ethmoid sinuses, and 3) the middle ear (Figure 1). Septic cavernous sinus thrombosis usually originates from suppurative infection of one of these draining structures, especially infec-
CLINICAL FEATURES OF SEPTIC CAVERNOUS SINUS THROMBOSIS

Onset often abrupt with severe headache, especially in and about the involved eye

Diplopia and ipsilateral visual impairment occur

Severe edema of virtually all soft tissue orbital structures is noted, including the cornea and conjunctiva, and the base of the nose. Proptosis, chemosis and engorgement of the superficial veins of the upper face are associated findings

Ophthalmoptlegia and a dilated, nonreactive pupil due to inflammation and ischemia of contiguous cranial nerves may complicate the picture. Retinal venous dilatation, hemorrhages, and papilledema are usually associated with visual loss or even total blindness

The cerebrospinal fluid may be hemorrhagic and under increased pressure

Usually shows pleocytosis (mononuclear and neutrophilic)

Protein concentration increased

Glucose concentration normal

If infection spreads to the subarachnoid space, abnormalities consistent with purulent meningitis will be present

Although symptomatology begins unilaterally, extension of infected thrombus to the contralateral sinus resulting in bilateral signs is common.

Figure 2.

tion caused by Staphylococcus aureus or Group A hemolytic Streptococcus. Pyodermal conditions of the upper face (the “triangle of death”) such as orbital cellulitis, paranasal boil, or erysipelas have been particularly implicated. In rare instances cavernous sinus thrombosis is purely aseptic and in such cases is usually a consequence of profound dehydration, local trauma, tumor, or a complication of surgery for tic douloureux.

The onset of septic cavernous sinus thrombosis is often abrupt. In addition to the signs and symptoms of an inciting local infection with systemic sepsisemia, the patient experiences severe headache, especially in and about the involved eye, diplopia, and ipsilateral visual impairment (Figure 2). Severe edema of virtually all soft tissue orbital structures, including the conjunctiva and cornea, and the base of the nose, may be associated with proptosis, chemosis and engorgement of the superficial veins of the upper face. Retinal venous dilatation, hemorrhages, and papilledema are usually associated with visual loss or even total blindness. The clinical picture is completed by ophthalmoplegia and a dilated, nonreactive pupil which result from inflammation and ischemia of anatomically contiguous cranial nerves. Although symptomatology usually begins unilaterally, extension of infected thrombus to the contralateral sinus, resulting in bilateral signs, is common. Pulmonary embolization complicates approximately 10 percent of cases. Infarction of the pituitary is a very rare but noteworthy complication.

Clinical entities most frequently confused with septic cavernous sinus thrombosis are uncomplicated orbital cellulitis, orbital tumor, and carotid-cavernous sinus fistula. (It should be stressed, however, that septic cavernous sinus thrombosis can complicate orbital cellulitis.) True ophthalmoplegia is rarely present in any of
SEPTIC LATERAL SINUS THROMBOPHLEBITIS ALMOST INVARIABLY ARISES FROM ACUTE OR CHRONIC MIDDLE EAR INFECTION

The lateral sinus receives extracranial drainage through emissary veins primarily from the overlying mastoid sinus. Rarely, involvement of the lateral sinus stems from a cutaneous infection of the lateral neck, or may follow an infection in the pharynx or teeth.

Figure 3.

these other conditions; diplopia in orbital tumor or cellulitis is caused by intraorbital mass effect and extraocular movements can be shown to be preserved although diminished in range. Moreover, orbital tumor and carotid-cavernous sinus fistula are not associated with infection or evidence of inflammation. Carotid-cavernous sinus fistula is also often characterized by a bruit and a widened pulse pressure on tonography.

While the cerebrospinal fluid in septic cavernous sinus thrombosis may be hemorrhagic and under increased pressure, and usually shows mononuclear and neutrophilic pleocytosis and an increase in the protein concentration, the glucose concentration remains in a normal range.

If infection has spread to the subarachnoid space, abnormalities consistent with purulent meningitis are present, including hypoglycorrhachia and the presence of microorganisms. Although clinical features usually permit ready diagnosis, objective confirmation can now be obtained in early or equivocal cases by carotid arteriography, retrograde internal jugular venography, or especially by the technique of orbital venography in which contrast medium is injected into the angular facial vein.

Septic lateral sinus thrombosis: The lateral sinus receives extracranial drainage through emissary veins primarily from the overlying mastoid sinus. Thrombosis, especially septic thrombophlebitis of this dural sinus, almost invariably arises from acute or chronic middle ear infection, primarily acute otitis media with associated mastoiditis (Figure 3). In rare instances the process stems from a cutaneous infection of the lateral neck, pharynx, or teeth. Interestingly, in acute cases Group A Streptococci have been implicated as the causative organisms four times more frequently than other organisms. However, Bacteroides species have predominated in cases of septic lateral sinus thrombosis related to chronic mastoiditis.

Major clinical features of septic lateral sinus thrombosis include signs of acute or chronic otitis or mastoiditis and evidence of a generalized increase in intracranial pressure, that
is, nausea and vomiting, headache, often above and behind the involved ear, lateral rectus palsy, and papilledema (Figure 4). Because of the pattern of intracranial venous drainage, lateral sinus thrombosis is most frequent (80 percent of cases) and symptoms tend to be more severe with right-sided involvement. Focal neurologic deficits are relatively rare. In severe cases the process can extend into the internal jugular vein which may become palpable as a tender cord; signs of damage to the ninth, tenth, and eleventh cranial nerves may then also become evident.

The diagnosis of septic lateral sinus thrombosis is suggested by the appearance of signs of sepsis and increased intracranial pressure in a patient with infective middle ear disease. Temporal lobe brain abscess must be excluded. Except for an elevated pressure the cerebrospinal fluid is commonly negative but may show abnormalities similar to those seen in cavernous sinus thrombosis. Angiography confirms the diagnosis of septic lateral sinus thrombosis.

Septic superior sagittal sinus thrombosis: Fortunately thrombophlebitis of the superior sagittal sinus is very rare. However, septic thrombosis of this structure in infants can be a consequence of severe dehydration and inanition, and blunt superior sagittal sinus thrombosis is well known historically as a complication of the puerperium. Septic thrombosis usually results from extension of thrombosis in the lateral or cavernous sinuses or from parasal supplicative sinusitis, primary meningitis, or contiguous osteomyelitis or other parameningeal infection.

Patients complain of severe headache and show evidence of delirium and signs of intracranial hypertension. When the process is extensive, and especially if it is posteriorly located, extension of thrombophlebitis to the cortical veins may result in infarction of underlying cortex and weakness and sensory loss which are most prominent in the legs. In severe cases Jacksonian seizures, dense hemiparesis, aphasia, and other extensive deficits are seen.

Cerebrospinal fluid findings in this disorder are similar to findings in other septic or venous thromboses. Sagittal sinus thrombosis is also best confirmed by angiography.

Septic thrombophlebitis of the internal jugular vein: In most instances septic thrombosis of the internal jugular vein develops as an extension of thrombosis in the lateral sinus. However, primary infective internal jugular thrombosis can arise from suppurative oropharyngeal infection in which event anaerobes, such as Bacteroides species, are predominant causative organisms. Recognition of this condition may be hindered by the paucity of local signs of jugular inflammation. Most patients present with cryptic sepsis, often associated with septic pulmonary emboli or septic arthritis.

**Diagnosis of Intracranial Septic Thrombophlebitis**

Intracranial venous thrombosis is most reliably confirmed by radiographic examination using one of the following techniques: 1) direct sagittal sinus venography (rarely performed in the present era), 2) study of the venous phase of carotid arteriography, or 3) orbital venography in patients with evidence of cavernous sinus thrombosis. Examination of the cerebrospinal fluid, radioisotope brain scans, and electroencephalography provide adjunctive information, but are not of specific diagnostic value; these diagnostic studies are probably of more importance in identifying unrelated or complicating conditions such as meningitis and brain abscess.

In all instances of suspected or proven intracranial septic thrombophlebitis it is imperative to first exclude associated meningitis. Associated meningitis may be primary, if the underlying infection is bacterial.
Table 1

ANTIMICROBIAL THERAPY IN SEPTIC THROMBOPHLEBITIS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin G</td>
<td>200,000 to 300,000 units per kg</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>100 to 400 mg per kg</td>
</tr>
<tr>
<td>Methicillin (or Nafcillin or Oxacillin)</td>
<td>100 to 200 mg per kg</td>
</tr>
<tr>
<td>Cefazolin*</td>
<td>100 to 200 mg per kg</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>50 to 100 mg per kg</td>
</tr>
<tr>
<td>Gentamicin* (or Tobramycin)</td>
<td>5 mg per kg</td>
</tr>
<tr>
<td>Clindamycin*</td>
<td>20 to 40 mg per kg</td>
</tr>
<tr>
<td>Carbencillin*</td>
<td>400 mg per kg</td>
</tr>
</tbody>
</table>

1. With the exception of gentamicin, which is usually given intramuscularly, all drugs should be administered intravenously in divided doses at intervals of 8 to 8 hours. However, if necessary (as in shock or coagulopathy), gentamicin can also be given intravenously if administered slowly (over > 15 minutes).

2. Recommended dosage if renal and hepatic function are normal; if renal and hepatic function are compromised, dosage should be modified appropriately.

3. Cefazolin and clindamycin are not recommended for intracranial septic thromboembolism, especially if associated meningitis is present.

4. In intracranial septic thromboembolism and meningitis caused by chloramphenicol-resistant and ampicillin-resistant Gram-negative bacilli, supplemental intrathecal gentamicin (1 to 4 mg per 12 hours) is recommended.

5. Carbencillin is recommended only for sensitive strains of Pseudomonas, indole-positive strains of Proteus and Enterobacter species.

Meningitis, or may be secondary due to extension of extrameningeal infection causing septic thromboembolitis to the subarachnoid space. Brain abscesses may also accompany septic intracranial thromboembolitis, or mimic it clinically, and must be excluded by brain scan or angiography.

Management of Intracranial Septic Thromboembolitis

Specific treatment of intracranial septic thromboembolitis consists of the following procedures: 1) surgical and antimicrobial therapy of the primary infection; 2) surgical evacuation of supplicative clot when necessary and feasible (usually restricted to the lateral and sagittal sinuses); and 3) treatment of associated seizures, intracranial hypertension, and fluid and electrolyte derangements. Elevation of the head and neck to a 45° angle has been recommended to promote venous drainage. Decompressive craniotomy may occasionally be required for refractory intracranial hypertension. Because of the possibility of precipitating hemorrhagic infarction, the use of anticoagulants remains controversial although some authorities have used them extensively and successfully without adverse effects. With the availability of effective antimicrobial therapy, surgical removal of thrombus is usually unnecessary. Septic thrombosis of the lateral sinus is anatomically most amenable to craniotomy and external drainage; ligation of the ipsilateral jugular vein is usually no longer recommended unless septic pulmonary emboli or refractory jugular thromboembolitis ensues. In primary septic thromboembolitis of the internal jugular vein, surgical ligation of the vein is necessary only when sepsis is refractory or embolization continues in the face of adequate medical therapy. Anticoagulation is definitely indicated for this condition.

Initial antimicrobial therapy should be guided, when possible, by Gram-stained smears and cultures of specimens from the inciting infection. If cultures are not available, therapy should include a penicillinase-resistant, semisynthetic penicillin such as methicillin. Isolations of the pathogen from the blood permit conclusive identification of the etiologic agent. Cephalothin or clindamycin should not be employed for septic intracranial thromboembolitis and should certainly never be used if active meningitis is present because of the very poor penetration of these drugs into the cerebrospinal fluid. Recommended dosages of antimicrobial agents in the treatment of septic intracranial thromboembolitis are listed in Table 1.

Prognosis

The outlook for survival and even complete recovery from septic intracranial thromboembolitis has improved markedly in the past 20 years. If the condition is recognized early and promptly treated, the majority of patients survive; residual neurologic deficits, even when severe, often fade or even disappear in time. A mortality rate of approximately 30 percent still attends septic cavernous sinus thrombosis and septic thrombosis of the sagittal sinus when it is associated with cerebral infarction. However, most patients with septic thrombosis of the lateral sinus survive and are left with surprisingly little residual effect.

Septic Pelvic Thromboembolitis

Bland versus septic pelvic thromboembolitis: Bland pelvic thromboembolitis is a relatively common complication of parturition or gynecologic surgery with or without associated intrapelvic infection 16,17 (Figure 5). It is characterized by fever with or without chills, lower abdominal and pelvic discomfort and tenderness, and occasionally by palpable ovarian (transabdominal, paramedian) or uterine (pelvic) venous cords. This entity usually continued on page 17
BLAND VERSUS SEPTIC PELVIC THROMBOPHLEBITIS: DIFFERENTIAL FEATURES

Bland Pelvic Thrombophlebitis
(Complicates parturition or gynecologic surgery with or without associated intrapelvic infection)

- Fever, with or without chills
- Recognized pulmonary embolism relatively infrequent with early anticoagulation
- Systemic effects less prominent
- Shock less common
- Septicemia not a feature
- Lower abdominal or pelvic discomfort and tenderness (ovarian or uterine cords occasionally palpable)

Figure 5.

Septic Pelvic Thrombophlebitis
(Nearly always associated with suppurative infection, most frequently postpartum endometritis, septic abortion, pelvic inflammatory disease, or postsurgical infection)

- Spiking fever, rigors
- Septic pulmonary embolism common
- Tachypnea; tachycardia (often exceeding 150 per minute)
- Hypotension (shock frequent)
- High grade septicemia (blood culture positive in one third of cases)
- Acute abdominal findings consistent with suppurative pelvic infection

sponds dramatically to anticoagulation—by prompt defervescence and diminution of pelvic symptoms, even after appropriate systemic antimicrobial therapy of an inciting infection has failed. Pulmonary embolism is relatively uncommon if early anticoagulation is initiated.

In contrast, true septic pelvic thrombophlebitis is nearly always associated with an inciting suppurative pelvic infection—most frequently postpartum endometritis, septic abortion, pelvic inflammatory disease, or postsurgical infection—and has far more serious clinical portent.\textsuperscript{18–21} The patient usually manifests signs of high-grade septicemia, often with shock, and commonly shows signs of septic pulmonary emboli. Tachycardia, often exceeding 150 per minute, and tachypnea, hypotension, spiking fevers, and rigors in concert with suppurative pelvic infection are virtually diagnostic. The presence of hypoxia and the finding of multiple pulmonary emboli on perfusion lung scan or angiogram confirm the diagnosis. Blood cultures are positive in about one third of patients; the predominant organisms are Group A Streptococci and Enterococci, Escherichia coli and other aerobic enteric bacilli, and especially anaerobic Streptococci, Bacteroides and Clostridium. A plain roentgenogram may disclose gas within the pelvic tissues which is associated with anaerobic Streptococci and aerobic bacilli as well as Clostridium.

Treatment of septic pelvic thrombophlebitis: Therapy must begin with antimicrobial agents and, when necessary, surgical treatment of the primary pelvic infection. Because transcervical intrauterine cultures may be nonrepresentative and blood cultures are often negative, needle aspiration of identified collections or the pelvic cul-de-sac is recommended in addition to cultures of the uterine aspirate and blood (Figure 6). All cultures must also be processed for anaerobes. Although specific antimicrobial therapy may be suggested by the results of Gram stained smears of clinical specimens, major pelvic infections are so frequently polymicrobial that initial antimicrobial therapy should be chosen for effectiveness against Streptococci, Clostridia, and both aerobic and anaerobic Gram-negative bacilli, regardless of the results of the smears.

In postsurgical infections, coverage against Staphylococcus aureus should also be considered. We prefer high doses of penicillin or ampicillin (methicillin or cephalothin) in combination with chloramphenicol, but a regimen of clindamycin and gentamicin has also proved to be effective. In critically ill patients the author employs three drugs: penicillin, gentamicin, and clindamycin. Recommended doses of antimicrobial agents are listed in Table 1.

Evacuation of the infected uterus by dilatation and curettage, or hysterectomy, may be required for severe
endometritis associated with shock, especially when Gram stain of a smear of intrauterine or cul-de-sac aspirate shows that Clostridium is the causative agent. If clostridial infection is strongly suspected or confirmed by Gram stain or culture and the patient is in shock and deteriorating, gas gangrene antitoxin should be administered and hyperbaric oxygenation may also be of benefit.

Septic thrombophlebitis involves the ovarian and the uterine veins in equal frequency, either individually or in combination. Consequently, surgical venous interruption for prevention of thromboembolism must be directed at both groups of veins to be effective.

On the basis of a large clinical experience Collins recommends ligation of the inferior vena cava and ovarian veins for septic pelvic thrombophlebitis with presumed or proven septic emboli \(^{18,20}\) (Figure 7). However, antimicrobial therapy and anticoagulation with heparin appear to be adequate as initial therapy for the average patient, with or without evidence of pulmonary embolization.\(^ {14,19,22}\) Surgical venous interruption is needed if the patient does not respond to medical treatment by defervescence and lessened pelvic inflammation within two to four days, or if the patient experiences pulmonary embolism during adequate anticoagulation.

**Pylephlebitis**

Septic thrombophlebitis of one or more tributaries of the portal vein, often including the main portal venous trunk, is invariably a consequence of severe, usually prolonged, intra-abdominal suppuration (Figure 8). The most frequently incriminated underlying conditions are acute appendicitis or unrecognized subacute periappendiceal abscess, diverticular abscess,\(^ {23}\) postsurgical intra-abdominal abscess, ulcerative colitis and regional enteritis, and, especially, obstructive ascending supplicative cholangitis. Portal venous thrombosis rarely leads to acute portal hypertension and the most frequent and greatly feared sequela of pylephlebitis is metastatic liver abscess.\(^ {24}\)

**Diagnosis:** Patients usually show signs and symptoms of an intra-abdominal supplicative infection but some patients, especially elderly patients, may show no evidence of such infection. Fever and chills are almost universal. Other signs that are usually present include mild degrees of jaundice, right upper quadrant pain and tenderness, hepatomegaly, and, occasionally, splenomegaly. These signs, in combination with an identified intra-abdominal focus of infection, strongly suggest the presence of pylephlebitis (Figure 9). Deeper jaundice, rigor, and shock with right upper quadrant tenderness must be regarded and managed as obstructive supplicative ascending cholangitis until proven otherwise.

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**IMPORTANT CONSIDERATIONS IN ANTIMICROBIAL THERAPY**

Blood cultures are often negative

Transcervical intrauterine cultures may be nonrepresentative

Needle aspiration of identified collections or the pelvic cul-de-sac are recommended

All cultures must be processed for anaerobes. Antimicrobial therapy may be suggested by Gram-stained smears of specimens, but major pelvic infections are so frequently polymicrobial that initial therapy should be chosen for effectiveness against *Streptococci*, *Clostridia*, and both aerobic and anaerobic Gram-negative bacilli. In postsurgical infections, coverage against *Staphylococcus aureus* should also be considered.

**Figure 6.**
SEPTIC PELVIC THROMBOPHLEBITIS WITH PRESUMED OR PROVEN SEPTIC PULMONARY EMBOLI MAY NECESSITATE LIGATION OF BOTH THE INFERIOR VENA CAVA AND OVARIAN VEINS

Antimicrobial therapy and anticoagulation with heparin appear to be adequate initial therapy for the average patient, with or without pulmonary embolization, but if defervescence and lessening of pelvic inflammation do not occur within two to four days or if the patient suffers pulmonary embolism during adequate anticoagulation, surgical venous interruption is indicated.

Figure 7.

Sudden massive ascites, shock, and hemorrhagic diarrhea herald complete portal venous occlusion with venous infarction of the bowel which is, fortunately, a rare complication. Suggestive but nonspecific laboratory findings are leukocytosis, often exceeding 20,000 per cu. mm., and low-grade elevations of bilirubin (2 to 5 mg. per 100 ml.) and alkaline phosphatase. Blood cultures are positive, usually for enteric Gram-negative bacilli (such as Escherichia coli or Klebsiella-enterobacter), Clostridia, or Enterococci in approximately 50 percent of patients when pylephlebitis is caused by supplicative cholangitis; blood cultures are positive for these organisms or anaerobic Streptococci or Bacteroides in approximately 50 percent of patients when pylephlebitis originates from nonbiliary intra-abdominal foci of infection. Polymicrobial bacteremia is not uncommon.

It is often difficult to distinguish between pylephlebitis and severe, nonphlebitic intra-abdominal infection because the diagnosis is primarily a clinical diagnosis. However, liver abscess must always be excluded by radioisotope scintigraphy of the liver.

Treatment of pylephlebitis: The originating intra-abdominal infection usually requires surgical drainage. Suppurative obstructive cholangitis, due mainly to biliary calculus and less frequently to tumor, is commonly associated with shock and constitutes a surgical emergency. If early surgical decompression of the obstructed common bile duct is not promptly effected, the mortality approaches 100 percent. In general, mortality is very high in pylephlebitis, especially if the patient is elderly or otherwise debilitated, or if hepatic abscesses have developed.

Initial antimicrobial therapy for suspected pylephlebitis is best tailored to the presumed intra-abdominal focus of infection, as follows: for pylephlebitis arising from nonbiliary intraperitoneal infections, a drug effective against Bacteroides fragilis should be included. Penicillin G, ampicillin, or cephalothin in combination with chloramphenicol, or clindamycin in combination with gentamicin is effective against most pathogens likely to be encountered. However, if obstructive cholangitis is suspected, gentamicin should be an integral part of the regimen because multi-resistant aerobic Gram-negative bacilli are present in about 25 percent of patients.

The long term drug regimen may be modified according to response to therapy and results of aerobic and anaerobic cultures of intra-abdominal abscesses and blood. Because of the ever present possibility of miliary liver abscesses in pylephlebitis, we urge continuation of parenteral antimicrobial therapy for at least one to two weeks after the local infection is controlled. Prolonged therapy serves to eradicate any residual microscopic foci of hepatic suppuration which could later develop into macroscopic liver abscesses. Anticoagulation is unnecessary because thromboses of the portal vein and its tributaries later undergo spontaneous recanalization.

Septic Thrombophlebitis as a Complication of Intravenous Therapy

One of the most serious complications of infusion therapy is septic thrombophlebitis which, in this setting, is also known as "suppurative phlebitis." Burn patients are particularly susceptible to suppurative phlebitis and this entity now rivals burn wound infection as a cause of death in burn patients. The unique susceptibility of burn patients probably stems from 1) the massive population of microorg...
organisms in anatomically proximate sites which can colonize the cannula wound directly or colonize the thrombus by bacteremic spread; 2) an associated generalized hypercoagulable state; and 3) masking of local and systemic signs of cannula-related infection by concurrent burn wound infection, which delays removal of the cannula. The organisms most frequently implicated in cases of suppurative phlebitis are coagulase positive Staphylococcus aureus and, since 1967, multiply-resistant Gram-negative bacilli, especially Klebsiella-enterobacter, Pseudomonas and Serratia. In the past two years the author has encountered three cases caused by Candida albicans.

**Septic Thrombophlebitis of Peripheral Veins**

It has been estimated that at least 30,000 cases of intravenous plastic catheter-related sepsis occur in this country each year but the catheter is not recognized as the source of infection in many of these cases. A number of independent clinical studies indicate that sepsis occurs in more than 2 percent of patients in whom the catheter is left in place for longer than 48 hours. Uncomplicated catheter-related sepsis usually responds rapidly to simple removal of the offending catheter, occasionally even without antibiotic therapy. In contrast, suppurative phlebitis—the extreme of cannula-related infection—is characterized by thrombopurulence and microorganisms within the venous lumen, which constitute an intravenous abscess. Unless the infected thrombus is identified and surgically excluded from the systemic circulation, sepsis usually persists despite antimicrobial therapy and the patient succumbs to unremitting septicemia. Suppurative phlebitis has usually been caused by plastic catheters left in place for more than 72 hours, but catheters left in place for less than 48 hours have also been incriminated (Figure 10). Moreover, we recently detected a case of suppurative phlebitis caused by a scalp vein needle. The saphenous veins appear to be most frequently involved although virtually any cannulated vein is susceptible.

**Diagnosis:** Signs and symptoms of sepsis commonly appear between two and 10 days after removal of the catheter. Local inflammation may be present, and ranges from slight tenderness to florid cellulitis with a palpable cord and purulent drainage. Although external evidence of inflammation or suppuration has been reported to be absent in up to 70 percent of burn patients with suppurative phlebitis, the
CLINICAL FEATURES OF PYLEPHLEBITIS AND ITS COMPLICATIONS

**Pylephlebitis**
- Mild degrees of jaundice
- Right upper quadrant pain and tenderness
- Fever and chills
- Hepatic enlargement (occasionally splenomegaly as well)

**Complete portal venous occlusion with venous infarction of the bowel**
- Severe abdominal pain
- Sudden massive ascites
- Shock

**Obstructive suppurative ascending cholangitis**
- Fever, rigors
- Deeper jaundice
- Shock

Signs and symptoms of intra-abdominal suppurative infection

Hemorrhagic diarrhea

Right upper quadrant tenderness

**Figure 9.**

Fact that most cases were identified postmortem may make this observation suspect. In the author’s experience and in published reports 32-35 suppurative phlebitis in the nonburn patient is usually associated with inflammation at the infusion site and, frequently, with expressible pus.

Strong clinical suspicion is most important in the diagnosis of suppurative phlebitis, especially if sepsis of uncertain etiology develops in a patient who is receiving intravenous therapy or who recently received intravenous therapy. Whenever a cannula (plastic catheter or steel needle) is removed the vein should routinely be milked toward the cannula wound, beginning two to three cm. proximally. The expression of pus, especially a ml. or more, strongly suggests the presence of a linear collection, almost certain

within the vein. All cannulas removed from critically ill patients should routinely be cultured if the cannula has been many days in situ or if signs of thrombophlebitis or systemic sepsis are present. We have found that rolling the amputated segment across a blood agar plate, in contrast to the conventional technique of culture in broth, provides a more accurate assessment of local infection.36

Even if the cannula was removed several days before the appearance of sepsis and the wound is closed, venous suppuration must still be considered in the patient with refractory sepsis without apparent source. The cutdown or percutaneous cannula wound can be reopened, at the bedside if necessary, and the vein milked in an attempt to express the pus. However, ideally the vein should be surgically exposed in the operating room to a distance at least several centimeters above the estimated former position of the cannula tip. Any thrombus thus obtained should be sent for immediate Gram stain, histopathologic examination, and semiquantitative cultures. The identification of infective suppuration, either grossly, histologically, by Gram stain, or by culture (heavy growth on an agar plate) establishes the diagnosis.

**Treatment of suppurative phlebitis:** Mild or early cases of suspected septic thrombophlebitis—characterized by the expression of minimal purulence at the time of catheter removal and the absence of signs of systemic sepsis—may possibly be treated effectively with systemic antimicrobial drugs alone.32,34 Initial antimicrobial therapy should be
based on the Gram-stained smear of material obtained from the vein. However, if Gram-stained smears are unavailable or microorganisms are not seen, the initial drugs should be selected for their activity against penicillinase-producing Staphylococcus aureus and multiply-resistant nosocomial Gram-negative bacilli. Combinations such as methicillin and gentamicin, or cephalothin and gentamicin are recommended.

For proven suppuration of the major extent associated with severe or persistent sepsis, surgical extirpation is the safest course and is the only effective treatment. Proximal ligation, incision and drainage of the involved segment has been reported to be effective.23 However, Pruitt and his colleagues,28-30 who have by far the greatest experience with this entity, strongly urge complete resection of the involved segment. The infusion site should be opened widely and the vein explored to a point above the highest level of gross involvement, as evidenced by transition from a dull gray external luster, palpable thrombus, and intravenous thrombopurulence to normal appearing vein and free flow of blood. Dissection should extend beyond the highest communicating tributary to the deep circulation which should be ligated. Complete excision of the entire involved purulent segment and, when feasible, all its involved tributaries, probably offers the best chance for cure. The rationale for total excision rather than ligation with or without drainage is the continued potential for blood seeding through anastomotic communications to the deep venous circulation that is associated with ligation.

**Septic Thrombophlebitis of the Great Central Veins**

Pruitt and his coworkers28 recently reported 25 instances of septic thrombosis of the great central veins in 139 burn patients. Three of the 25 specifically involved the superior
vena cava, nine involved the subclavian vein, and 13 involved the iliofemoral veins. All were associated with indwelling plastic catheters used for total parenteral nutrition, venous pressure monitoring, or for conventional intravenous therapy. In addition to a clinical picture of refractory sepsis, septic pulmonary emboli were demonstrated at postmortem in one third of patients. Septic pulmonary emboli were detected antemortem in only two patients, both with septic thrombosis of the subclavian vein. Both patients manifested swelling of the ipsilateral upper extremity and the diagnosis was confirmed angiographically. However, most patients showed no external evidence of venous obstruction or inflammation.

Even more recently, Popp and his coworkers in the Cincinnati Shriners Burn Institute reported 16 cases of bacteremia and fungemia related to catheters used for total parenteral nutrition in burned children, including five fatal cases of superior vena cava septic thrombosis. All of these latter cases occurred in children with full-thickness burns involving the subclavian areas, necessitating central venous cannulation through peripheral veins or the burn wound. All five cases had endocarditis, four with Candida, at autopsy.

It is likely that septic thrombophlebitis of the great central veins is also relatively common in nonburn patients and simply has not been considered clinically during life or sought at the autopsy table.

When this disastrous complication of central venous cannulation is suspected, venography can help to establish the diagnosis. Suppuration of the iliofemoral or distal subclavian veins can be successfully managed by systemic antibiotics, anticoagulants, and, if necessary, by surgical ligation, as recently shown by Vic-Dupont and his colleagues. In contrast, involvement of the proximal subclavian vein or superior vena cava must be managed with anticoagulants and high doses of intravenous antibiotics. Surgical debridement of septic clot in the proximal subclavian vein or superior vena cava might be considered in individual cases but no published experience exists to support or guide its use. Recent published reports and the author's own experience document only one survivor among ten patients with septic vena cava thrombosis identified during life and treated with antimicrobics alone.

**Prevention of Septic Thrombophlebitis**

*Associated with local infection:* Septic thrombophlebitis associated with local infection can be most effectively prevented if the physician appreciates the great susceptibility to this complication of patients with focal infections in certain anatomic areas such as the upper face, para nasal sinuses, middle ear, and pelvis. All infections, especially infections of these anatomic areas, must be promptly treated.

*As a complication of intravenous therapy:* Ideally, suppurrative phlebitis should be very rare in the nonburn patient; the incidence of cannula-related sepsis can be greatly decreased by stringent attention to an established program of local asepsis. Most importantly, venous cannulas, especially plastic catheters, should be removed within 48 to 72 hours, whenever possible, and should be removed immediately upon the development of local inflammation, unexplained fever, or sepsisemia without apparent source. The dismal prognosis of suppurrative phlebitis of the great central veins demands a program of prevention which limits the duration of catheterization with central venous catheters. In the thermally injured patient, strict limitation of the duration of venous cannulation appears to be the most important single measure in lessening the incidence of venous suppuration.

**References**