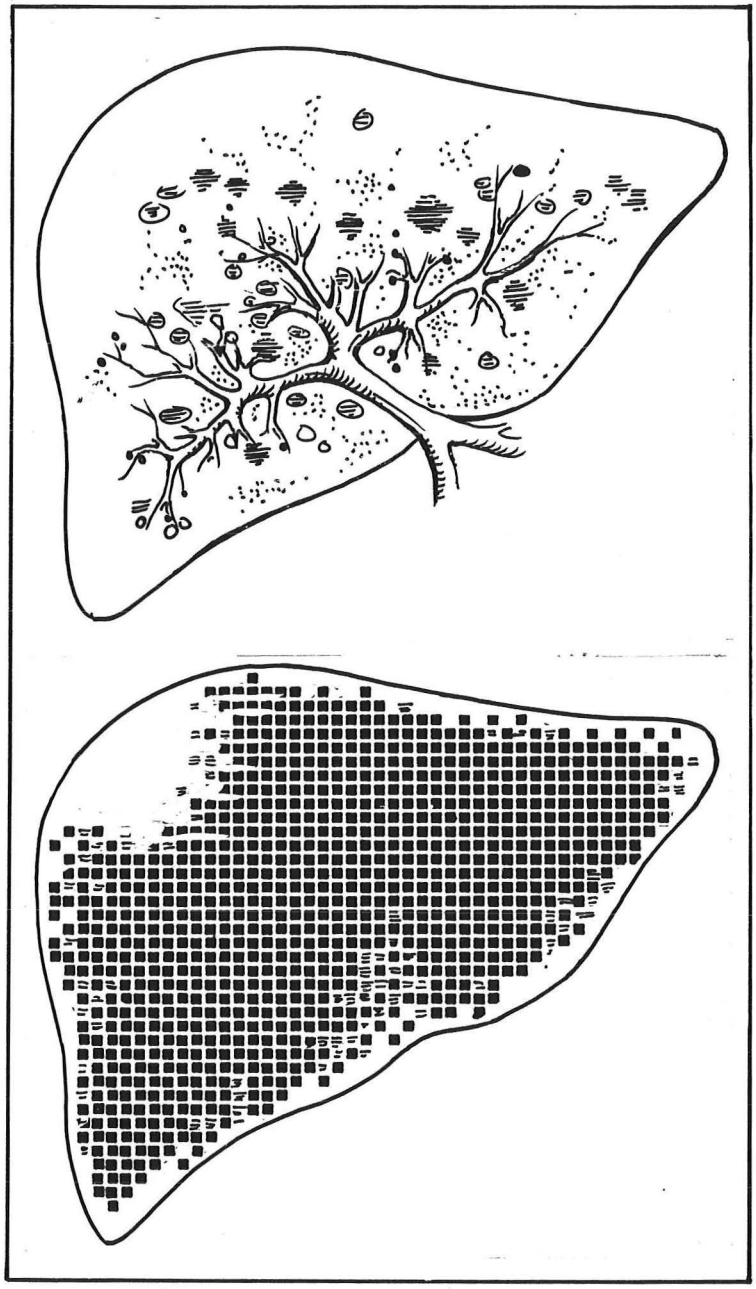
Hepatic Abscess



Medical Grand Rounds
28 May, 1981
Jennifer A. Cuthbert, M.B. B.S.

"...the chief aid to the diagnosis of hepatic abscess is the knowledge that it may occur..."

Taylor, 1902: Guy's Hosp Rep 56:109

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Case History #1

This 21 year old black male presented with a 4 day history of malaise, anorexia, fever and back pain. These symptoms increased 2 days before admission and he also had diarrhea. On examination he was febrile (103.8°C) and icteric, the liver was 13 cm in overall span, 5 cm below costal margin and tender. Chest examination revealed dullness at the right base.
Admitting laboratory tests: Hb 13 g/dl, WCC 10,400/mm^3, bilirubin 2.5 mg%, SGOT 450 IU, alk. phos. 160 IU, albumin 3.5 g/dl, globulin 3.6 g/dl, PT +2.5 secs.
Chest x-ray: Right pleural effusion.
He was admitted to the medicine service and further investigations obtained.
Ultrasound examination: defect in right lobe, probable abscess.
Liver-spleen scan: avascular mass in right lobe, shunting.
Blood cultures: positive for Klebsiella.
He was treated with multiple antibiotics and transferred to the surgery service. He remained febrile for a further two days and then underwent exploratory laparotomy. No primary focus was found in the abdomen. There were adhesions at the dome of the liver on the right and on breaking these down an abscess cavity was entered. He had drainage of the abscess by a 12th rib resection approach. Post-operatively his fever gradually abated. He was followed in clinic until discharge.
Comment: This patient presents the classic syndrome of fever and tender hepatomegaly. He responded well to surgical drainage.

Case History #2

This 22 year old LA male presented to the Emergency Room approximately 1 week before admission with a three day history of vomiting, he was also febrile (101.2°C) but left without being seen. He returned complaining of fever, nausea, vomiting and abdominal pain. He had a history of heavy alcohol consumption. On examination he had a liver span of 14 cm, tenderness over the liver and an epigastric mass.
Admitting laboratory tests: Hb 15.6 g/dl, WCC 18,600/mm^3, bilirubin 0.7 mg/dl, SGOT 134 IU, alk. phos. 110 IU, albumin 4.0 g/dl, globulin 3.4 g/dl, PT +2.5 secs. Chest x-ray normal.
He was thought to have possible alcoholic liver disease.
The following investigations were obtained:
Liver-spleen scan: avascular defect in left lobe
abnormal uptake on Gallium scan
Ultrasound examination: large cystic left lobe defect
A provisional diagnosis of amoebic abscess was made and he was treated with metronidazole. He rapidly became afebrile. On follow-up in hospital there was decrease in size of the defect by both sonography and radionuclide scan. He did not attend for follow-up after discharge. His IHA test was positive: 1:4096.
Comment: This patient presented with fever, tender hepatomegaly and an epigastric mass due to an abscess in the left lobe. He did well with conservative therapy.

Case History #3

This 38 year old Pima Indian woman was admitted for non-union of the left tibia and on questioning gave a one month history of right upper quadrant pain. On physical examination she was febrile and tender in the right upper quadrant. Examination of the chest was normal.
Admission laboratory tests: Hb 7 g/dl, smear microcytic hypochromic, WCC 5,500/mm^3, platelets 625,000/mm^3, ESR 155; bilirubin 1.7 mg/dl, SGOT 66 IU, alk. phos. 336 IU, albumin 2.2 g/dl, globulin 5.1 g/dl, PT +2 sec, amylase 458.
In hospital her Hb fell to 4 g/dl and a direct Coombs test was positive with a cold antibody in the serum. The combination of anemia and high ESR were thought to be due to sepsis or autoimmune disease with underlying myeloma or collagen vascular disease. Diagnostic investigations were obtained to follow-up the abnormal liver function tests.
SPEP: polyclonal γopathy, γ globulin 2.7 g/dl.
Liver-spleen scan: patchy defect in left lobe ? extrahepatic, splenomegaly, shunting
Ultrasound examination: No abscess seen, ? gallstones.
A provisional diagnosis of acute cholecystitis and possible ascending cholangitis was made with an abscess not excluded. She was treated with antibiotics but remained febrile. At laparotomy an intrahepatic abscess involving both lobes of the liver was found. There were no gall stones.
Culture of the abscess contents grew α hemolytic streptococci and anaerobic strep. intermedius. Gram-negative rods, seen on initial stain, did not grow in culture.
Following drainage of the abscess her course was uncomplicated and on discharge she had normal laboratory tests. Retrospective analysis of the ultrasound examination demonstrated an abscess and gas pockets in the liver were the cause of acoustic shadowing interpreted as gallstones.
Comment: This chronic presentation had almost no signs or symptoms suggesting hepatic abscess. Investigation was complicated by secondary abnormalities and misinterpretation of primary abnormalities.

Case History #4

This 29 year old Latin American male presented with a 3 week history of productive cough, hemoptysis and pleuritic right-sided chest pain. He also complained of sweats and a 25 lb weight loss. On examination he was febrile (104°C), with tenderness over the right lower chest wall, there was dullness at the right base with rales. The abdomen was non-tender with a liver span of 12 cm and 5 cm palpable below the costal margin.
Laboratory tests: Hb 11 g/dl, WCC 17,700/mm^3, ESR 98, bilirubin 0.4 mg/dl, SGOT 70 IU (nl <72), alk. phos. 143 IU, albumin 3.5 g/dl, globulin 4.5 g/dl.
Chest x-ray: Right hilar adenopathy, cavity
Blood gases: pO_2 86, pCO_2 31
A diagnosis of anaerobic lung abscess was made and he was treated with IV antibiotics. A liver-spleen scan and sonogram were ordered to investigate his hepatomegaly and elevated alk. phos. On the second hospital day he developed acute right upper quadrant tenderness. The following results were obtained:
Liver-spleen scan: Right lobe avascular defect
Ultrasound examination: 5 cm defect right lobe
He was treated with metranidazole 750 mg tid for 10 days with prompt response. His serology for amoeba returned positive at 1:1024. Repeat sonogram demonstrated a decrease in size of the abscess cavity. He was seen once in follow-up.
Comment: This patient had extension of the amoebic abscess into the right lung and presented with apparent primary pulmonary disease. This responded well to metronidazole and did not require drainage.

Case History #5

This 36 year old Latin American male presented with a 2-3 week history of right upper quadrant pain and gastrointestinal symptoms including anorexia, nausea, vomiting and diarrhea. He had also noticed dark urine and weight loss of 25 lbs. He was admitted with a diagnosis of hepatitis.
On admission he was noted to be febrile, icteric and abdominal examination revealed tender hepatomegaly, with a span of 18-20 cm. Chest examination was normal.
Laboratory tests: Hb 12.5 g/dl, WCC 8,400/mm^3, bilirubin 2.1 mg/dl, SGOT 250 IU (nl <40), alk. phos. 222 IU, albumin 2.4 g/dl, globulin 1.9 g/dl, PT +3 secs.
Ultrasound examination: multiple defects in both lobes. Serameba: strongly positive.
After sonography he was commenced on metronidazole 750 mg tid. He soon developed increased abdominal pain with peritoneal signs and was transferred to surgery. He underwent exploratory laparotomy and was found to have ruptured a superficial left lobe abscess with development of acute peritonitis. This abscess and 4 additional ones were drained. His post-operative course was complicated by persistent fever despite a 21 day course of metronidazole and drainage; therefore chloroquine was added. He also had a recurrent right pleural effusion (Serameba positive) which required drainage with a thoracostomy tube. At discharge his laboratory tests were Hb 10.7 g/dl, WCC 11,500/mm^3, bilirubin 0.4 mg/dl, SGOT 27 IU, alk. phos. 438 IU, albumin 2.9 g/dl, globulin 3.8 g/dl, PT +1 sec.
The IHA returned from the C.D.C. <1:64, and remained negative on repeat examination x6; however when tested at PMH, the indirect hemagglutination assay was positive.
Comment: This patient illustrates hepatic presentation, peritonitis after rupture of a left lobe abscess and false negative IHA.

Case History #6

This 53 year old black male was seen in the Emergency Room two days before admission with a 5 day history of fever, right upper quadrant pain and the recent onset of arthralgias and peripheral oedema. On examination he was febrile, had mild right upper quadrant tenderness, the liver was 12 cm in span and smooth. His oral hygiene was poor and he had marked periodental disease. Five teeth were extracted and he was given penicillin and topical therapy. He was brought back to the ER two days later, having been found by the Dallas Fire Department in a state of collapse. His examination was unchanged except for deterioration in mental function.
Admitting laboratory tests: Hb 6.9 g/dl, WCC 6,000/mm^3, platelets 25,000/mm^3, bilirubin 2.3 mg/dl, SGOT 415 IU, alk. phos. 312 IU, amylase 626, albumin 2.0 g/dl, globulin 2.2 g/dl, PT +3.5 secs.
In hospital his WCC rose to 16,900/mm^3, his platelet count fell to 2,000/mm^3 and his PT prolonged. He had evidence of rhabdomyolosis (CPK 1535), bone marrow revealed toxic changes. The following diagnostic investigations were obtained:
KUB: air over liver ? abscess
Chest x-ray: normal
Ultrasound examination: defect in right lobe ? malignancy, ?? abscess
Blood cultures: positive for E.coli
He was treated with multiple antibiotics and then underwent laparotomy and drainage of the abscess cavity after deterioration in his condition. There was no evidence of rupture. E.coli grew from cultures of the abscess cavity and histopathologic specimens confirmed the presence of an abscess but also revealed hepatoma and necrosis in the area. His post-operative course was extremely complicated and he eventually died 6 weeks after admission.
Comment: This patient illustrates the diagnostic helpfulness of the simple plain abdominal x-ray. He also demonstrates that necrotic areas of liver are liable to become infected.

HISTORICAL ASPECTS

Hepatic abscesses have been recognized since the time of Hippocrates. His observation was "When abscess of the liver is treated by cautery or incision, if the pus which is discharged be pure and white, the patients recover; but if it resembles the lees of oil as it flows, they die." Despite this ancient recognition, liver abscess complicating dysentery was not described until 1828 and the clinicopathologic entity of pyogenic liver abscess was not recorded until John Bright's description in 1836. Bright wrote of the post-mortem finding of multiple abscesses in a 61 year old female with gallstones and in a 47 year old tailor with pus in the portal vein. Further understanding of the etiology of pyogenic liver abscess was gained with the description by Waller in 1846 of pylephlebitis complicating appendicitis. Numerous case reports of pyogenic abscess were published during the latter half of the 19th century.

Physicians of the time were also aware of tropical liver abscess but the link between amoebic dysentery and amoebic liver abscess could not be made until after the identification of the causative organism. The first description of amoebic dysentery and the pathogenic organism associated with it was by Lösch in 1875. Eventually it was realized that there were two major forms of dysentery, bacillary and amoebic, and that liver abscesses were associated with the amoebic type.

Since then, both pyogenic and amoebic infections of the liver have continued to occur. The present report will review the recent literature and compare this to the local experience.

PREVALENCE: Pyogenic Abscess

The prevalence of pyogenic hepatic abscess has been estimated from both autopsy and hospital admission data. Since 1900, there has been little change in the frequency of liver abscess at autopsy (Table 1).

Table 1

PREVALENCE OF PYOGENIC HEPATIC ABSCESS

Author		Source	#	Prevalence
Baerensprung	1875	Autopsy	7,326	1.47%
Kobler	1901	Autopsy	17,204	0.45%
Collins	1932	Autopsy	18,300	0.61%
Sherman and Robbins*	1932-1958	Autopsy	21,945	0.59%
Gruhn and Cohen	1938-1962	Autopsy	3,253	1.11%
de la Maza et al.*	1959-1968	Autopsy	9,489	0.57%
Rubin et al.	1961-1973	Autopsy	12,517	0.29%

*Mallory Institute of Pathology, Boston, MA.

Similarly, if the prevalence of pyogenic liver abscess is assessed in comparison to the number of hospital admissions, the prevalence is likewise unaltered in the past 100 years (Table 2). Thus, it appears that the use of antibiotics, sophisticated diagnostic equipment and improved surgical techniques has altered neither the occurrence nor the outcome of pyogenic abscess.

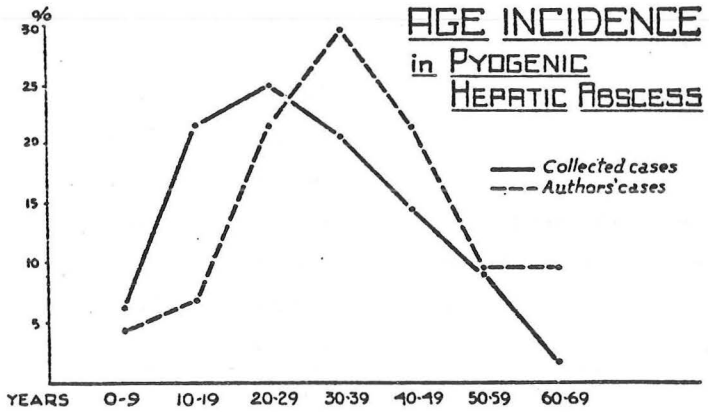
Table 2

PREVALENCE OF PYOGENIC HEPATIC ABSCESS

Author		Source	#	Prevalence
Dudley	~1870-1890	Admission	28,034	0.04%
Norris and Farley	~1901-1925	Admission		0.04%
Ochsner et al.	1928-1937	Admission	540,776	0.008%
Rubin et al.	1961-1973	Admission	345,456	0.016%
Pitt and Zuidema	1952-1972	Admission	615,385	0.013%
Perera	1980	Admission	53,330	0.03%

The autopsy data has changed in other respects if not in frequency. The patient population today is considerably older. In addition, associated diseases, particularly malignancies, are much more common in recent series. Ochsner in 1938 reported a shift in age prevalence from the twenties to the thirties with a declining association of complicated appendicitis and hepatic abscess (Fig I). More recently, many series report an average age between 50 and 60 years.

Figure I



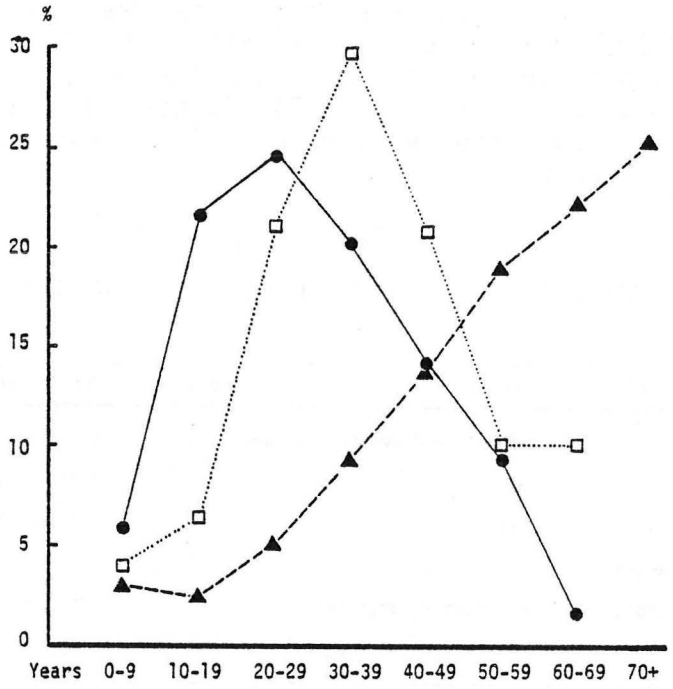
Comparative age incidence in 518 collected cases and 47 authors' cases.

From Ochsner et al. (1938)

Since 1966, 16 of 17 reviews have included patients whose ages ranged to the eighth decade or beyond (Fig II). Neoplastic diseases were not an etiologic factor in the younger patients of Ochsner et al., nor was an association noted in his extensive review. More recently, malignant biliary tract obstruction with subsequent ascending cholangitis and multiple abscess formation in older patients has become more common. Post-operative pyogenic abscess may also complicate other intra-abdominal cancer surgery.

Figure II

AGE INCIDENCE IN PYOGENIC HEPATIC ABSCESS



Comparative age incidence in 518 collected cases (●—●) and 47 authors' cases (□··□) Ochsner et al. (1938) and 378 collected cases (▲--▲) published since 1960.

Reports prior to 1938 indicated a male predominance among patients with pyogenic liver abscess. Current series indicate little difference (M:F = 1.7:1 since 1966). The reason for the earlier inequality is unclear but may be related to bias in the hospital population or to incidence of autopsy permission. The recent equalling of the sex ratio has been attributed to the increased frequency of biliary tract disease among women; however, complicated biliary tract disease exhibits little preference.

PREVALENCE: Amoebic Abscess

Amoebiasis is found world wide. The prevalence of amoebic liver abscess is dependent upon both the frequency and characteristics of amoebiasis in a given geographic area. Forty years ago, the prevalence of amoebiasis in the United States was estimated at 10%, now it is less than 4%. Endemic foci within the U.S. are associated with poor sanitation and have been reported from Indian reservations, from lower socioeconomic areas and from mental institutions. In addition, the frequency of detecting cysts and trophozoites in random samples of stool or sigmoidoscopically obtained smears will vary with the experience and diligence of the laboratory (see also microscopy). Outside the U.S., particularly in tropical countries, there is a much higher prevalence of amoebiasis. In Mexico, for example, it has been estimated that 15-30% of the total adult population is affected. Table 3 illustrates the results of surveys for intestinal amoebiasis in several countries. A longitudinal survey in The Gambia, West Africa showed a near 100% infection rate over one year, despite failure of attempts to recover cysts in the environment.

Table 3

RESULTS OF SURVEYS FOR INTESTINAL AMOEBIASIS IN SEVERAL COUNTRIES

Country	Centre	Prevalence	Population
U.S.A.	Central and Southern States	1.5%	Hospital patients
	New Orleans	6.4%	Accident victims
India	Delhi	9.7%	Cross-section
Australia	Queensland	1.0%	Urban
Gambia	Up-country, dry season	13.7%	Village
	Coastal, rainy season	52.3%	Urban

Liver abscess, the most common extraintestinal manifestation of amoebiasis, has been reported in a varying percentage of patients with invasive amoebiasis. In the collected series of autopsy cases reported by DeBakey and Ochsner in 1951, the incidence of hepatic involvement ranged from 7.6% to 84.4%, with an average of 36.6%. There was also considerable variation in the reported incidence of hepatic involvement in clinical cases of intestinal amoebiasis, from less than 1% to more than 25% with an average incidence of 8.1% for the entire collected series (Table 4). DeBakey and Ochsner found an incidence of hepatic involvement in 11.1% of clinical cases of amoebiasis admitted to the Charity Hospital in New Orleans.

Table 4

INCIDENCE OF HEPATIC INVOLVEMENT IN AMOEBIASIS

Source			Invasive Amoebiasis	Hepatic Amoebiasis	Incidence
Collected series	to 1951	Autopsy	5,250	1,925	36.6%
		Clinical	16,582	1,352	8.1%
New Orleans	1928-1947	Clinical	1,923	214	11,1%
South Africa	1955-1974	Clinical	5,087	2,074	40.8%

These differences depend in part on the classification of the type of hepatic involvement, with increased reporting of so-called amoebic hepatitis in the latter part of DeBakey and Ochsner's collected series. In South Africa, researchers believe the incidence of intestinal amoebiasis is decreasing while that of hepatic amoebic abscess is remaining unchanged. Their diagnosis of abscess is proven in the majority of cases by aspiration of contents as a routine therapeutic regimen. This persistent occurrence of amoebic liver abscess in the presence of decreased intestinal amoebiasis may be due to the variable latent period between initial exposure to the pathogenic organism and presentation with amoebic abscess. The number of cases of amoebic abscess being diagnosed at Parkland Memorial Hospital has increased since May, Lehmann and Sanford reported the local experience from 1943 to 1966 (Table 5). They found 15 cases of amoebic liver abscess and 24 cases of pyogenic abscess during that 24 year period. Landay and co-workers recently reported sonographic findings in 27 patients diagnosed in a little over 4 years. The incidence of amoebic liver abscess at the University of Texas Medical Branch in Galveston has remained constant. They reported 37 cases between 1946 and 1966 with an additional 15 cases between 1966 and 1976. The increase in incidence of liver abscess at Parkland Memorial Hospital may reflect both awareness of the possible occurrence of the disease and the availability of expert diagnostic capabilities.

Table 5

INCIDENCE OF AMOEBIC LIVER ABSCESSES

Hospital		Admissions	Liver Abscess	Incidence
New Orleans	1928-1937	510,800	118	1/4,300
	1938-1947	530,400	96	1/5,400
Korea	1956-1962	5,619	22	1/255
Atlanta	1950-1963	582,541	23	1/25,600
Phillipines	1952-1967	~570,000	120	1/4,750
Dallas	1943-1966	NA	15	NA
	1975-1979	~150,000	33	1/4,500

A marked preponderance of males is noted in almost all series of amoebic liver abscess. In some reports this is due to the inclusion of military personnel with a predominantly male hospital population. In others, the majority of cases are derived from immigrant workers, as in the recent local experience. Studies based on an unselected urban or rural population have also found an unequal sex ratio.

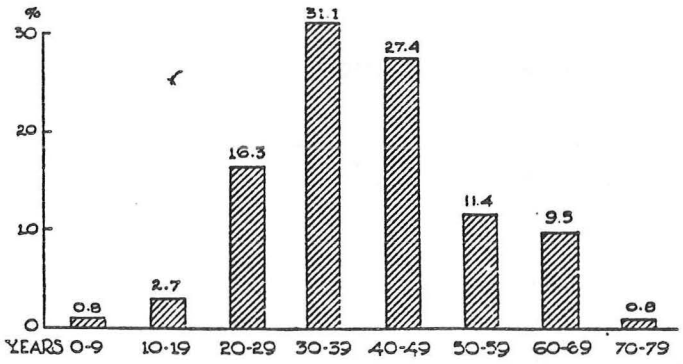
Table 6

SEX RATIO IN AMOEBIC LIVER ABSCESS

Author		# Cases	M:F Ratio
DeBakey and Ochsner	Collected Series	2522	14:1
	New Orleans	263	5:1
Mehta and Vakil	Urban, India	158	11:1
Crone et al.	Rural, Korea	200	7:1
Bieler et al.	Urban, South Africa	247	4:1
Tsai	Rural, Taiwan	2322	7:1
May et al.	Dallas 1943-1966	15	14:1
Landay et al.	Dallas 1975-1979	27	26:1

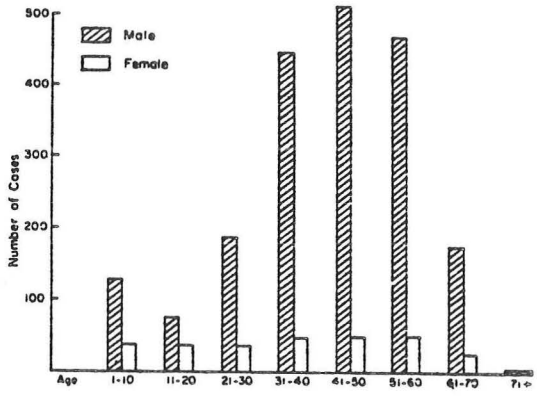
There is no explanation for the predominance of males in virtually all reported series of amoebic abscess. The unequal sex ratio in invasive intestinal amoebiasis is not as marked. One possibility is that estrogens may increase the efficiency of clearance of foreign and particulate matter by the mononuclear phagocyte system and endothelial cells in the liver. Experimental evidence to support this hypothesis comes from the increased rate of hepatic clearance of particles found in rats given pharmacological doses of estrogen.

Figure III



Age incidence in hepatic amebiasis in the authors' series of 263 cases.

From DeBakey and Ochsner (1951)



Age-sex incidence of amebic liver abscess.

From Tsai (1973)

As a group, patients with amoebic liver abscess are younger than those with pyogenic abscess. Since 1966, the average age in most series of amoebic abscess has been between 30 and 40 years (mean 33 years) and fewer than 20% are more than 60 years of age (Fig III). This is in contrast to the average age of patients with pyogenic liver abscess (51 years) and up to half the patients in some series are over the age of 60 years. The younger age of patients with amoebic abscess is not merely due to the age of the general population in tropical countries. Similar findings have been reported in the U.S. and here at Parkland Memorial Hospital (Table 7). Between 1975 and 1979, however, 5 of 9 patients at PMH with pyogenic abscess were 21 years of age or younger and the oldest patient was 60 years old.

Table 7

AGE OF PATIENTS WITH HEPATIC ABSCESS:

EFFECT OF ETIOLOGY

		Amoebic Abscess	Pyogenic Abscess
May, Lehmann and Sanford	1943-1966	15 cases	24 cases
		mean age 41 yrs	mean age 52 yrs
recent collected cases	1974-1979	33 cases	9 cases
		mean age 36 yrs	mean age 30 yrs

Amoebic liver abscess does occur in the pediatric age group, the youngest patient at PMH being 8 months old. Most of the cases in endemic areas are in children less than 3 years of age (Table 8). Of interest, the male predominance is less marked in the few available reports but this may be spurious due to the small number of cases.

Table 8

PEDIATRIC AMOEBIC LIVER ABSCESS

Author			# Cases	<3 yrs	M:F
Scragg	1951-1958	Durban, S.A.	53	91%	1.65:1
McCarty et al.	to 1973	Review	274	77%*	N.A.
Rode et al.	1963-1978	Cape Town, S.A.	27	67%	1.25:1
Harrison et al.	to 1979	Tucson, AZ	7	86%	0.17:1
Dykes et al.	to 1980	Charleston, SC	3	100%	2.00:1

*calculated from available information, excluding Scragg, 1958.

N.A. = Not available

ETIOLOGY AND PATHOGENESIS: Pyogenic Abscess

Normally, the liver is sterile and one of its major functions is the clearance of foreign and particulate matter from the portal venous system. This includes clearance of bacteria and other infectious agents, which gain access from the non-sterile intestine. The relative rarity of liver abscess complicating ulcerative colitis and regional enteritis illustrates the efficiency of this clearance mechanism under ordinary and extraordinary circumstances.

ETIOLOGY OF PYOGENIC LIVER ABSCESS

1. Biliary Tract Infection - cholangitis
   - secondary to benign or malignant obstruction
2. Portal Pyaemia - with or without pylephlebitis
   - diverticulitis, enteritis, colitis, appendicitis
3. Direct spread from contiguous infection - cholecystitis, perforation
   - subphrenic, perinephric, subhepatic abscess
4. Systemic hematogenous spread - via hepatic artery
5. Trauma - blunt or laceration
6. Intrahepatic disease - cyst, tumor, infarction

Pyogenic liver abscess occurs when an overwhelming number of bacteria enter the liver, generally being seeded from an intra-abdominal source with entry to the liver via the biliary tract or portal venous system (Table 9). Alternatively, systemic spread of extra-abdominal infection to normal or pathologic livers can result in formation of pyogenic abscess.

Table 9

ETIOLOGY OF PYOGENIC ABSCESS

Source of Infection	Before 1938*	After 1954†
	(percentage incidence)	
Portal	44	22
Biliary Tract	14	33
Systemic	13	13
Trauma	3	3
Miscellaneous	8	8
Cryptogenic	17	21

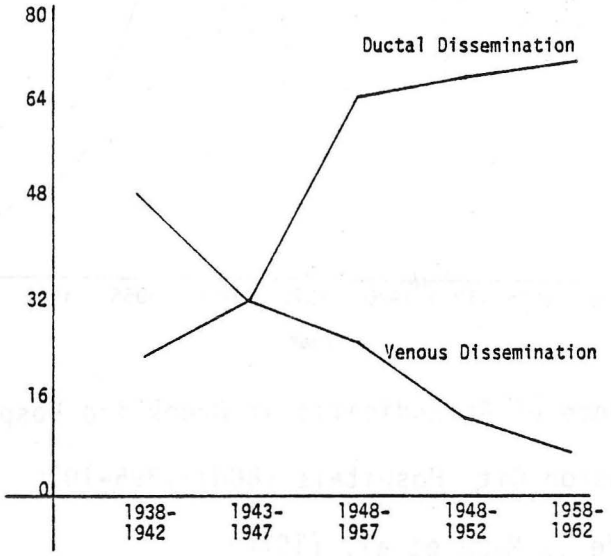
*From Ochsner, DeBakey and Murray, 1938, n=575

†From McDonald and Howard, 1980, n=885

In most recorded series, intra-abdominal infection is the major recognizable source for pyogenic liver abscess and spread occurs via the portal vein or biliary tract, depending on the actual site of infection. There has been a change in emphasis in recent years with an increasing proportion of cases being secondary to ascending cholangitis complicating biliary tract obstruction (Fig IV, Table 9).

Figure IV

DISTRIBUTION OF DUCTAL AND VENOUS DISSEMINATED ABSCESSES DURING DIFFERENT PERIODS

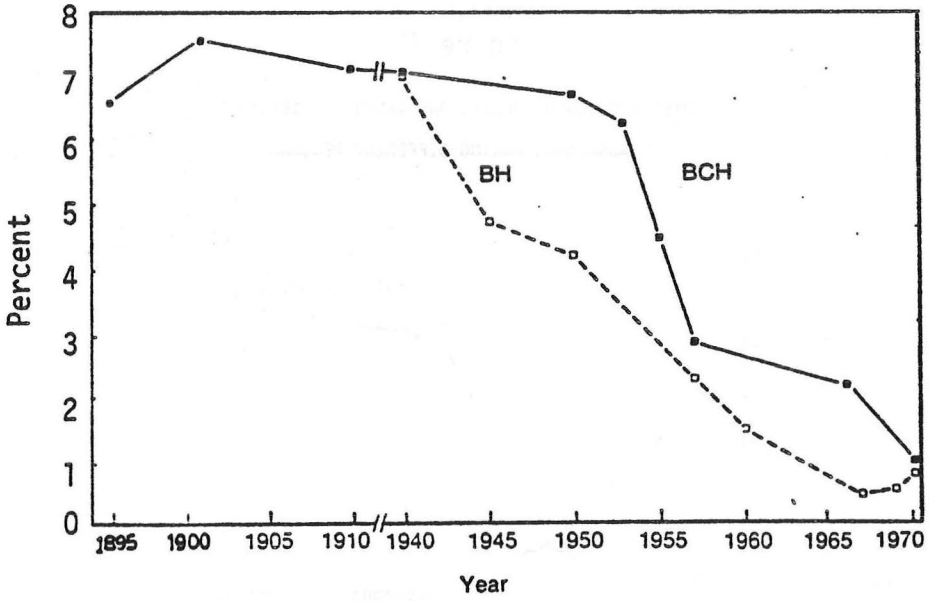


From Gruhn and Cohen (1965)

Much of the increase in biliary tract obstruction has been due to occurrence of malignant obstruction from carcinoma of the pancreas, bile duct or periampullary region. The decrease in portal venous infection has mainly been a decrease in liver abscess complicating appendicitis. An over-estimation of the importance of portal pylephlebitis secondary to suppurative appendicitis may have occurred in the past. The collected series of Ochsner, DeBakey and Murray reported that 34.2% of pyogenic abscesses were complications of appendicitis. Many of the individual reports represented the authors' interest in pylephlebitis and liver abscess. The original cases of Ochsner et al. contained 5 patients (10.6%) with liver abscess following appendicitis. Before the advent of antibiotic therapy, liver abscess or suppurative pylephlebitis was found in 0.3-0.4% of all cases of appendicitis. Since the improvement in surgical techniques and the introduction of appropriate antibiotic therapy, this complication has become rare. Furthermore, the overall incidence of appendicitis has decreased (Fig V). In 17 reports from 1970 to 1980, appendicitis was the source of infection in 7 of 566 cases of pyogenic liver abscess (1.2%) and a portal venous source of infection was implicated in 18.6%. Gastrointestinal

surgery, diverticulitis and pancreatitis are now major causes of intra-abdominal infection leading to pyogenic abscess. In the neonate, umbilical vein catheterization is an important source of sepsis which may lead to pyogenic liver abscess.

Figure V



Incidence of Appendicitis at Brookline Hospital (BH)

and Boston City Hospitals (BCH) 1895-1970

From de la Maza et al. (1974)

Pyogenic abscess has also been reported complicating a variety of diagnostic and therapeutic manipulations of the liver. These include liver biopsy, percutaneous transhepatic cholangiography and hepatic artery ligation. Liver biopsy may result in hematoma formation and local parenchymal cell necrosis with subsequent secondary infection. Similarly, following hepatic artery ligation, tumor infarction or hepatic sickling, necrotic tissue may become infected. Trauma with necrosis and/or hematoma has been reported as the cause of pyogenic abscess in up to 24% of cases in some series. Two of nine patients at PMH from 1975-1979 developed abscesses following trauma. Pyogenic abscess can also complicate other liver diseases. It has been reported in cirrhosis, necrotic tumor, hydatid and simple cysts. Amoebic abscesses, before or after treatment can become secondarily infected. In some patients no underlying cause may be detected and cryptogenic abscesses account for over half the cases in some series. Five of 9 recent patients at PMH had no demonstrable cause.

Factors producing diminished resistance to bacterial contamination probably play a major role in the etiology of many hepatic abscesses. Diminished host resistance may be found in the presence of biliary tract obstruction and neoplasia. In recent series, there has been an increase in the proportion of older patients with neoplastic disease (Table 10). The cancer is often the cause of the liver abscess (e.g. malignant biliary tract

obstruction, secondary infection of necrotic intrahepatic tumor) or it may result in compromise of normal defense mechanisms (e.g. after intensive chemotherapy, in the presence of widespread metastatic disease).

Table 10

NEOPLASTIC DISEASE ASSOCIATED WITH PYOGENIC ABSCESS

Author	# of cases	% incidence	obstruction
Pyrtek and Bartus	19/61	31	19/19
Joseph et al.	11/61	18	3/11
Lazarchick et al.	13/75	17	10/13
Rubin et al.	18/50	36	11/18
Pitt and Zuidema	22/80	28	18/22

*Number of cases with neoplasm having malignant biliary tract obstruction

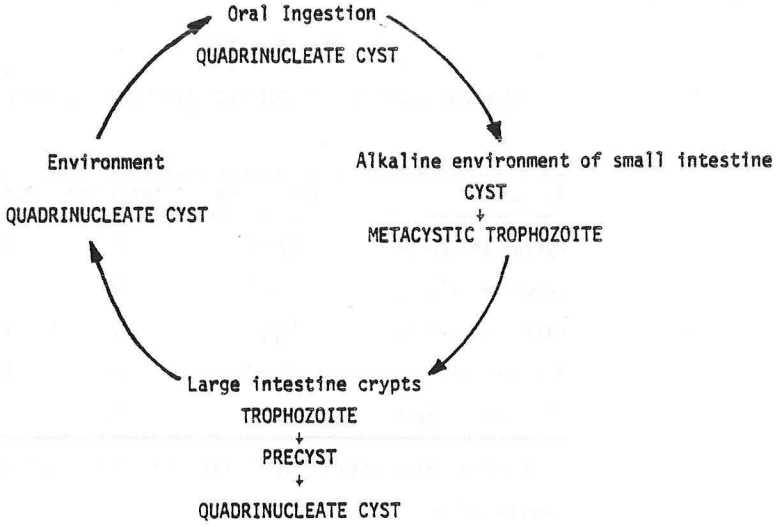
In children, pyogenic liver abscess is reported with leukemia and in chronic granulomatous disease, both of which are accompanied by diminished host resistance. Another cause of decreased host response is diabetes mellitus which has been reported in up to 25% of cases of pyogenic abscess, often with an increased mortality. Severe sepsis can also result in a poor response to infection as well as causing hematogenous spread to the liver. The commonest sources of septicemic liver abscess are renal, pulmonary and endocardial infections.

Pyogenic abscesses may be solitary or multiple (see Table 11). Biliary tract origin is more likely to cause multiple small abscesses and an acute presentation. Cryptogenic abscesses, by contrast, are often solitary and chronic in presentation. Solitary lesions occur more commonly in the right lobe, at least in part because of its increased bulk. Multiple abscesses are found in both lobes.

ETIOLOGY AND PATHOGENESIS: Amoebic Abscess

Amoebae are normally found in the large intestine of many hosts. Of those species which are parasitic in man, almost all are non-pathogenic since they lack the ability to invade tissue. Entamoeba histolytica, the organism causing intestinal and hepatic amoebiasis, is the major exception. The life-cycles of all amoebae are similar to that of E.histolytica (Fig VI). Man is the reservoir of E.histolytica and passes the infection to other primates, cats, dogs and rarely pigs.

Figure VI



The non-motile cysts are 10-20μ in diameter and have 1-8 nuclei (usually 4). Infection only occurs with ingestion of cysts, because unlike trophozoites, the cysts are resistant to gastric juice, to chlorine concentrations commonly used in domestic water purification, to room temperature and to drying. Cysts are found in both asymptomatic carriers and in invasive intestinal amoebiasis. The trophozoites (vegetative form) are motile, 12-50μ in diameter with a single nucleus and granular cytoplasm. The finding of trophozoites does not diagnose invasive amoebiasis since they may also live as a harmless commensal in the bowel lumen.

The factors that determine whether ingestion of E.histolytica cysts will produce disease, or not, are poorly understood. The following hypotheses have been suggested:

1. Virulence-producing amoebic-bacteria relationship: E.histolytica was not invasive in germ-free guinea pigs.

2. Virulence-producing amoebal viruses: No consistent changes found.

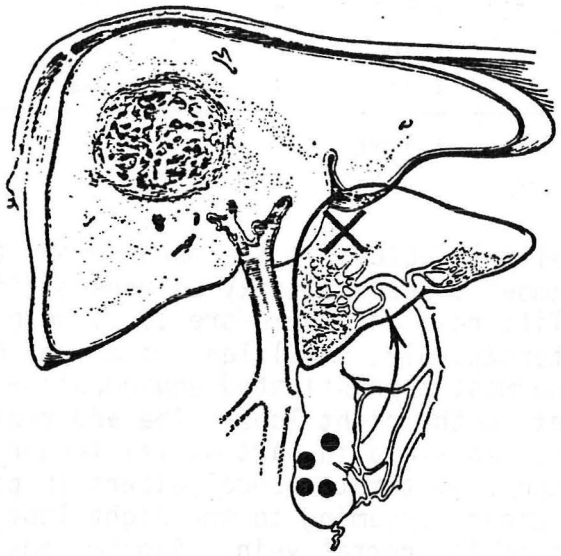
3. Amoebal lytic enzymes: E.histolytica produce pepsin-like and trypsin-like enzymes and do not produce a trypsin-inhibitive agent; invasive strains contain a different isoenzyme of phosphoglucomutase.

4. Host operative factors.

The existence of two or more morphologically indistinguishable species of amoebae might explain the presence of either the disease or the asymptomatic carrier state. Before characterization of E.hartmanni, asymptomatic carriers of this amoeba of low pathogenicity were diagnosed as E.histolytica cyst carriers. More recently, non-pathogenic strains of E.histolytica have also

been described. They are distinguished by differences in physico-chemical and growth characteristics. This possibility of pathogenic and non-pathogenic strains may explain the low prevalence of invasive amoebiasis in The Gambia despite a very high incidence of cyst passing. Nearby in Sierra Leone, 3-4% of medical admissions are for amoebiasis and more than half the patients have amoebic liver abscess. Amoebae reach the liver in the portal venous system but the pathogenetic mechanisms for abscess formation are not fully known and the latent period between the intestinal infection and the hepatic involvement is unexplained. In some cases corticosteroids given for unrelated disease have resulted in the development of amoebic abscess. Corticosteroids may also hasten the pathogenic process when given for misdiagnosed ulcerative colitis and chronic active hepatitis.

Figure VII



Pathogenesis of Amoebic Liver Abscess

In the large intestine, E.histolytica organisms come into direct contact with epithelial cells and hydrolytic enzymes released from surface lysosomes dissolve the limiting membrane of the larger cells. The amoebae then ingest the cells and eventually being surrounded by a lytic area. This process allows penetration of venules and passage to the liver where the amoebae lodge in smaller intrahepatic radicles of the portal vein (Fig VII). Lytic action then allows the organisms to break through the walls of the portal vein radicle and invade the connective tissue of the portal triad and the parenchyma. It is believed that most trophozoites entering the liver are destroyed by non-specific mechanisms such as a cytopathogenic effect from activation of complement components. The hepatic parenchymal cell is not primarily infected and therefore there is not a "hepatitis". Rather, the parenchymal cells are attacked by the same cytolytic process which occurs in the intestinal wall. This results in small areas of liquefaction necrosis bordered by fibrous strands and a minimal mononuclear infiltrate which extends concentrically. Invasion can occur along open veins and intrahepatic portal thrombosis and infarction may accompany the process. Coalescence of multiple small lesions produces larger macroscopic areas of necrosis. In acute disease there is no capsule to the abscess and rapid extension into surrounding parenchyma

can occur. Amoebae are found near the advancing edge of the lesion rather than in the necrotic center. Characteristically abscesses are solitary and in the right lobe (Table 11).

Table 11

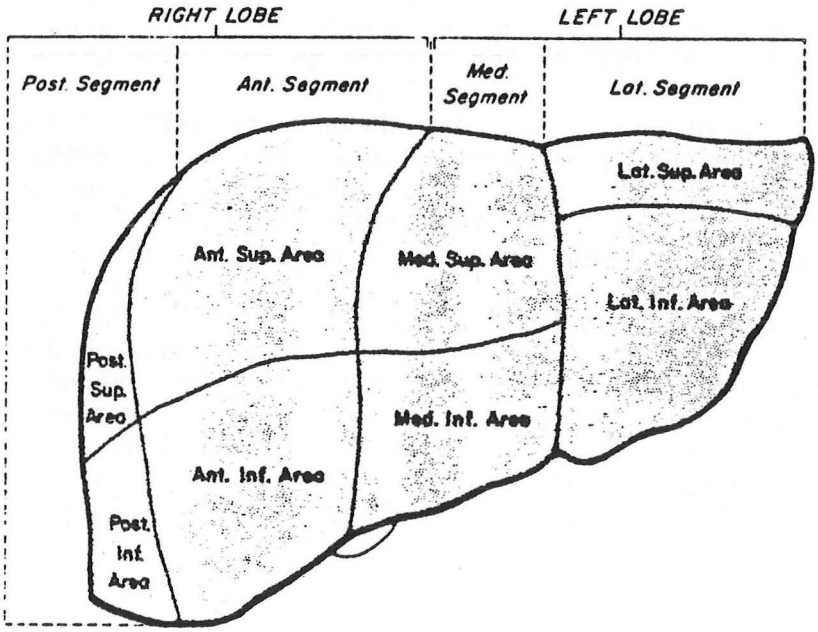
NUMBER AND SITE OF HEPATIC ABSCESSES*

	Pyogenic Abscess #	%	Amoebic Abscess #	%
Solitary	245/488	50	637/715	89
Multiple	243/488	50	78/715	11
Right Lobe	97/179	54	701/864	81
Left Lobe	21/179	12	97/864	11
Both Lobes	61/179	34	66/864	8

*Collected series (1966-1980)

In autopsy series multiple abscesses are more common (in 3 series 118/230 or 51%). Multiple amoebic abscesses may be more difficult to diagnose or have a higher mortality rate and therefore could be over-represented in autopsy series. Alternatively, small lesions may be overlooked or not detected (by even the most sophisticated equipment) when a large lesion is clinically present in the right lobe. The apparent predilection for the right lobe may be explained in part by its larger size. Some investigators have found asymptomatic cecal ulcers in patients with amoebic liver abscess and propose streaming to the right lobe in the superior mesenteric component of the portal vein. Another possible explanation is that anatomic divisions into lobes are not used, in favor of the easier falciform ligament division, the right side then being considerably more than half of the liver (Fig VIII).

Figure VIII



From Neiman and Goldstein (1975)

Abscess cavity size varies from a few centimeters to 20 cm in diameter and may contain up to 3000 ml of material. Classically the abscess contents are described as fluid which is either chocolate brown or like anchovy paste. This is due to necrosis of parenchymal cells and similar material can also be seen in the center of necrotic tumors. Sometimes the material is thinner and yellow or greenish. The fluid is odorless and sterile unless secondarily infected. As suggested above, E.histolytica are seldom found in the fluid but their detection is enhanced if one examines the final drops aspirated rather than the initial aspirate.

CLINICAL FEATURES

When hepatic abscess is the primary disease, the classic presentation is with abdominal pain, fever and tender hepatomegaly. In both pyogenic and amoebic abscesses the presentation can range from an acute illness with signs and symptoms of toxicity to a chronic disease of insidious onset. The abdominal pain is frequently described as a dull aching sensation in the right upper quadrant. It may increase with respiration and radiate to the right shoulder or laterally to the chest wall, presumably depending on the location of the abscess in the liver. Fever, when present, is persistent in the range of 38-39°C in amoebic abscess. High or spiking fevers are more often found with pyogenic abscess or a secondarily infected amoebic abscess. Clinical manifestations in pyogenic abscess may be referable to the abscess itself or to the underlying primary disease such as intra-abdominal infection or malignancy. The major symptoms (in descending order of incidence) were fever, pain, rigors, nausea and vomiting, weight loss, anorexia and malaise in a recent review of pyogenic liver abscess (Table 12).

Table 12

Presenting signs and symptoms of 490 patients with pyogenic hepatic abscesses.

	Number	Percent
Symptoms		
Fever	398	81
Pain	252	51
Rigors	174	36
Nausea and vomiting	164	33
Weight loss	155	31
Anorexia	132	27
Malaise	96	20
Signs		
Hepatomegaly	246	50
Tenderness	246	50
Jaundice	131	27
Abnormal chest x-ray	87	18

From McDonald and Howard (1980)

Less frequently reported symptoms included diarrhea, distension, pruritus, dyspnoea and intractable hiccoughs. There are no specific symptoms for either hepatic or pyogenic liver abscess. Diarrhea has been reported with pyogenic abscess, although less frequently than in amoebic abscess. The duration of symptoms at presentation is extremely variable, from a few days to more than a year. In general, patients with multiple pyogenic abscesses tend to have a shorter course before hospitalization. They more often present with septicemia or biliary tract obstruction than do those patients with a large solitary abscess.

Physical findings in pyogenic abscess are also non-specific. As shown above, tender hepatomegaly was present in approximately half of the patients. Jaundice was noted in 27% of patients and when present was associated with an especially poor prognosis. Findings less commonly observed were splenomegaly, mental status changes, ascites and abdominal mass or distension. The major signs and symptoms of pyogenic abscess have changed little over the years. However, in the collected series of Ochsner, DeBakey and Murray reported in 1938, tender hepatomegaly was a much more prominent finding than in McDonald and Howard's recent series (Table 13).

Table 13

PYOGENIC LIVER ABSCESS

Clinical Feature	before 1938* n = 286	n = 47	after 1954† n = 490
	(percentage incidence)		
Fever	96	94	81
Pain and tenderness	93	91	51
Hepatomegaly	89	62	50
Chills	59	36	36
Jaundice	36	25	27

*Collected series and authors' series, Ochsner, DeBakey and Murray (1938)

†Collected series, McDonald and Howard (1980).

One possible explanation is that the discrepancy is due to inclusion of amoebic abscesses in the older collected series, since tender hepatomegaly is very common in hepatic amoebiasis. The authors' own series (n=47) has a considerably lower incidence of hepatomegaly than does the collected series. Alternatively, the disease process may have resulted in less hepatomegaly in recent series because of early presentation with multiple abscesses of biliary tract origin.

The usual onset and presentation of amoebic liver abscess is with abdominal pain, fever and tender hepatomegaly, with symptoms present for less than 30 days (Table 14). Occasionally, there may be low grade chronic symptoms for months or years. This variety is now relatively rare in the United States where there is a higher index of suspicion. Six patients of 33 seen at PMH (1975-1979) had been symptomatic for 1 1/2 to 6 months.

Table 14

SYMPTOMS IN AMOEBIC LIVER ABSCESS

Symptom	No. of Patients*	Percent	Range
Pain	1287/1425	90	72-100
Fever	1139/1425	80	54-94
Malaise and weakness	174/330	53	33-95
Chills and rigors	311/662	47	20-71
Weight loss	210/564	37	4-100
Anorexia	154/534	29	2-80
Nausea and vomiting	129/480	27	18-47
Dyspnoea and cough	315/1390	23	6-50

*From 15 reports, totalling 1425 patients, published between 1966 and 1980.

Variability in selection and reporting by individual authors probably accounts for the wide range encountered for some symptoms. Studies reported from the United States were little different from those outside the U.S. Amoebic liver disease may present with symptoms very suggestive of respiratory infection. Patients may complain of fever with cough, dyspnoea, and pleuritic chest pain; only subsequently does abdominal disease become apparent. The Pulmonary service at PMH admitted 7 of the 33 recent patients. Occasionally patients present acutely, with symptoms simulating cholecystitis or appendicitis or they may have peritonitis following intra-abdominal rupture of an abscess. A few cases have been described with only fever and hepatic encephalopathy on presentation. In these patients, hepatomegaly was also present. Diarrhea has been reported in 10-55% of patients with amoebic abscess at the time of presentation, however, not all the diarrhea is amoebic in origin (see Table 30). Evidence of current amoebic infestation is found in 0-75% of cases. Many patients have neither past nor present history of symptomatic intestinal amoebiasis. Lamont and Pooler (1958) sought a history of intestinal amoebiasis in 200 patients and 110 (55%) specifically denied diarrhea, let alone dysentery.

Table 15

SIGNS IN AMOEBIC LIVER ABSCESS

Sign	Number of Patients*	Percent	Range
Hepatomegaly	1145/1425	80	47-95
RUQ tenderness	1231/1425	86	70-97
Jaundice	154/1253	12	3-38
Abnormal chest examination	448/1253	36	16-71

*From 15 reports, totalling 1425 patients, published between 1966 and 1980.

The physical findings in amoebic abscess are similar to those in pyogenic abscess (Table 15). The liver is generally smooth, diffusely enlarged and tender. Both lobes may be enlarged, even with an abscess confined to one lobe. Compensatory hypertrophy has been suggested to explain this finding. Enlargement may not be detected by palpation if it occurs upwards into the chest rather than below the costal margin. There is often localized tenderness, presumably coinciding with an underlying superficial abscess. The hepatic consistency may be hard, simulating cirrhosis or hepatic carcinoma. Splenomegaly was detected in 14% of cases and ascites in 10% of cases in a series with advanced liver disease. Amoebic liver abscess in the cirrhotic liver is uncommon although both diseases may be frequently found in certain environments. Jaundice occurs infrequently in most series of amoebic liver abscess. It has been found when multiple small abscesses are present and this combination has a poor prognosis. In addition it can occur with large solitary abscesses obstructing major bile ducts in the portal hepatis or when most of the normal liver tissue is replaced by a number of large abscesses.

Table 16

THORACIC AMOEBIASIS

Manifestation	Percent*
Hepatobronchial fistula	47
Pleural effusion and empyema	29
Lung abscess	14
Consolidation	10

*n = 146, considerable overlap

From Adams and MacLeod (1977).

Chest examination reveals rales, decreased breath sounds, dullness to percussion and other features of an effusion in many patients (Table 16). Hemoptysis occurs in patients with rupture of an abscess into a bronchus and sputum may have the appearence of anchovy paste. May, Lehmann and Sanford reporting the local Dallas experience in 1967 found that there was a statistically significant increase in the incidence of abnormal chest findings, pleuritic chest pain and diarrhea in amoebic liver abscess when compared with pyogenic abscess. The incidence of jaundice, in contrast, was decreased. Barbour and Juniper in Arkansas also found an increased incidence of clinical chest abnormalities in patients with amoebic abscesses, but abnormal chest x-rays were reported with equal frequency. Amoebic abscess unlike pyogenic abscess has not changed in its usual presentation since DeBakey and Ochsner's description in 1951.

ATYPICAL PRESENTATION OF HEPATIC ABSCESS

A. Amoebic or Pyogenic

1. F.U.O.
2. "Silent" abscess + hepatomegaly
3. Extrahepatic: extension beyond liver
4. Acute hepatic failure
5. Metastatic abscess

B. Amoebic

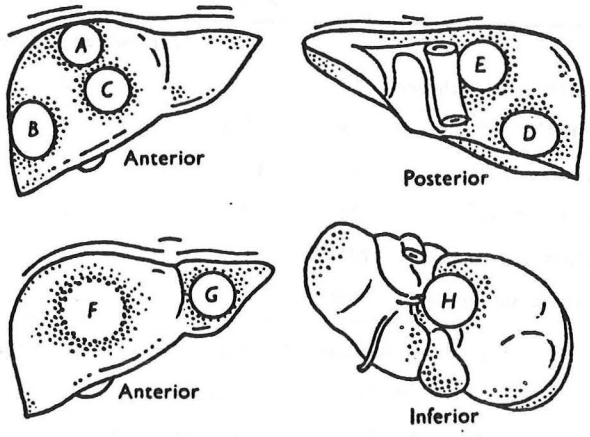
1. Acute amoebic dysentery

C. Pyogenic

1. Amyloidosis

Atypical presentations can occur in both pyogenic and amoebic liver abscesses. The commonest of these are as a fever of unknown origin or as a "silent" abscess, with or without hepatomegaly. The site of the abscess within the liver influences the mode of presentation (Fig IX). Abscesses in almost any site can present classically or as an insidious process or following rupture. Intrathoracic rupture occurs from the superior surface as does pericardial involvement.

Figure IX



Classic syndrome, Silent abscess, Intraperitoneal rupture: A-G

Intrathoracic rupture: A, B, F, G Pericardial rupture: G

Obstructive jaundice: H F.U.O.: F Budd-Chiari: E

Since the introduction of antibiotics, the incidence of extrahepatic complications from pyogenic abscess has not substantially altered, at first glance (Table 17). The decrease in thoracic involvement is balanced by an increase in localized spread above and below the liver. However, since 1975 there have been no reports of rupture into the peritoneum or thorax in nearly 250 cases. The persistence of complicating subphrenic and subhepatic abscesses may be due to 1° infection with contiguous spread involving the liver secondarily, thus suggesting some improvement since the commencement of antibiotic therapy.

Table 17

COMPLICATIONS OF PYOGENIC ABSCESS

	Ochsner et al. <1938	Collected Series >1950
Peritonitis	33/453 (7.2%)	16/251 (6.4%)
Intra-thoracic rupture	69/453 (15.2%)	12/251 (4.8%)
Subphrenic or subhepatic abscess	18/453 (3.9%)	33/251 (13.1%)

Amoebic abscesses can also present with extension beyond the liver or this may occur during the observed course of the disease. Perforation of the diaphragm and extension into the pleural cavity, lung or bronchial tree occurs in up to 20% of patients (Table 18). Intra-abdominal extension can occur with perforation of the stomach, colon or biliary tract or more commonly by free rupture into the peritoneal cavity. Occasionally a subhepatic collection occurs rather than generalized peritonitis. The outcome varies with local experience, therapeutic regimen and the general health of the patient, all of which are varied in the geographic locations represented in Table 18.

Table 18

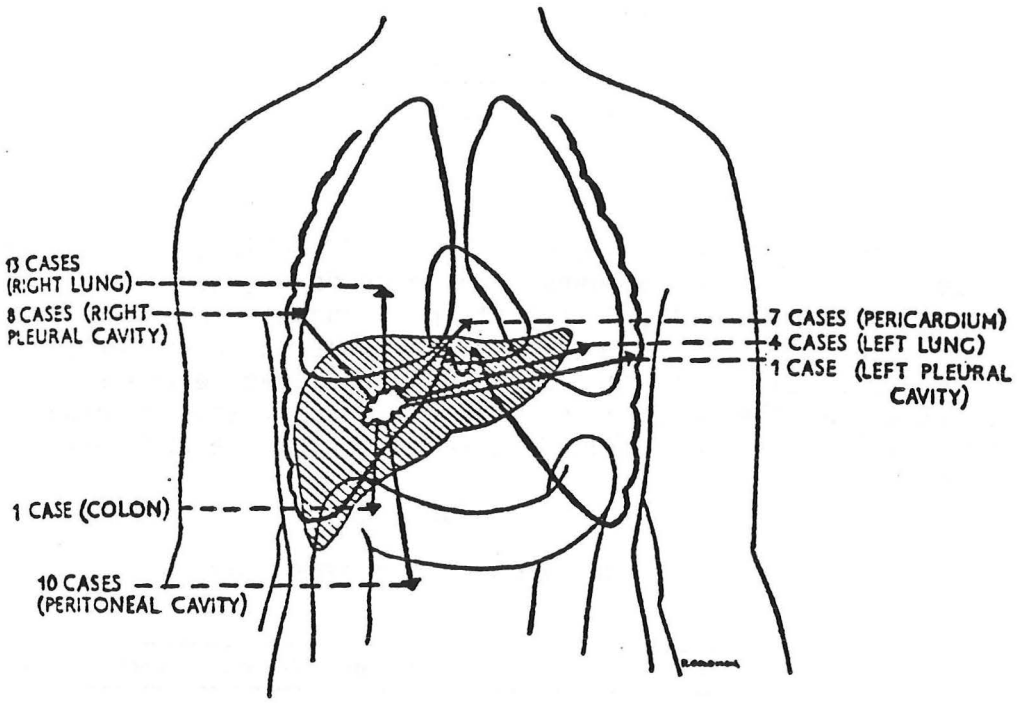
COMPLICATIONS OF AMOEBIC ABSCESS

Author	#Patients	Site of Rupture		
		Peritoneum	Thorax	Pericardium
		(percentage incidence)		
DeBakey and Ochsner	176	9	20	0.6
Turrill and Burnham	66	1.5	18	1.5
Licad and Recio	120	11	8	
Crane et al.	200	13	7	1.5
Adams and MacLeod	2074	1.8	7	1.3
Lamont and Pooler	250	4	10	3

Note: DeBakey and Ochsner (1951) and Turrill and Burnham (1966): U.S.; Licad and Recio (1969): Phillipines; Crane et al. (1972): Korea; Adams and MacLeod (1977) and Lamont and Pooler (1958): South Africa.

Left lobe hepatic abscess occurs far less frequently than involvement of the right lobe and accounts for <20% of cases. However, left lobe abscesses have a high incidence of rupture, because of the smaller mass of the left lobe, less typical presentation (epigastric rather than RUQ pain) and consequent delayed diagnosis. Because of their anatomical site, the abscesses frequently rupture or extend in the pericardial sac or pleural cavity (Fig IX, X).

Figure X



From Lamont and Pooler (1958)

Pericardial involvement in amoebic abscess progresses through three stages. Initially (presuppurative phase) there is a non-purulent pericardial effusion when the pericardium and diaphragm are involved in an inflammatory reaction. A purulent pericarditis occurs after rupture of the abscess through the diaphragm. Even if this is successfully treated, constrictive pericarditis may follow. The occurrence of chest pain, pericardial friction rub, pericardial effusion or signs of tamponade demands prompt therapeutic intervention. Aspiration of left lobe abscesses, in addition to medical therapy, may avoid such complications. Drainage of both the pericardial sac and liver abscess are essential once the effusion is purulent.

Table 19

AMOEBIC PERICARDITIS

	# Patients	Pre-suppurative	Suppurative
Collected series	34	4	30
mortality	19/34	0/4	19/30
Authors' series	25	5	20
mortality	8/25	0/5	8/20

From MacLeod, Wilmott and Powell (1966).

Secondary infection can complicate amoebic abscess in up to 40% of cases (Table 20). Spiking or persistent high fever, accompanied by a leukocyte count greater than 20,000/mm^3 strongly suggest this complication. Bacterial infection must also be considered if there is rapid deterioration without signs of extension of the abscess or a delayed response to therapy. Abscess cavities can also become infected after aspiration or drainage. To prevent this, all precautions should be taken during the procedure.

Table 20

SECONDARY INFECTION IN AMOEBIC ABSCESS

Author	# Patients	Percentage Infection
DeBakey and Ochsner (1951)	176	22
Lamont and Pooler (1958)	106	12
Licad and Recio (1969)	120	12
Crane et al. (1972)	200	37

DIAGNOSIS

The diagnosis of hepatic abscess is dependent upon demonstrating structural changes in the liver parenchyma and appropriate bacteriology (pyogenic) and serology or microscopy (amoebic abscess). Routine laboratory tests are usually non-specific (Table 21) with leukocytosis (>10,000/mm^3), mild anemia (<12 g/dl), elevated serum bilirubin (>1 g/dl), elevated serum alkaline phosphatase and decreased serum albumin (<3 g/dl). Similar abnormalities occur in both pyogenic and amoebic abscesses.

Table 21

LABORATORY FINDINGS IN HEPATIC ABSCESS*

	Pyogenic Abscess #	Pyogenic Abscess %	Amoebic Abscess #	Amoebic Abscess %
Leukocytosis	351/468	75	911/1232	74
Anemia	192/392	49	527/947	56
Hypoalbuminemia	144/223	65	165/227	73
↑ serum alkaline phosphatase	258/419	62	493/863	57
↑ serum transaminase	156/313	50	307/822	37
↑ bilirubin	160/336	48	241/983	25

*Collected series 1966-1980

HEMATOLOGY

The blood count may show a variable leukocytosis ranging from 5,000/mm^3 to over 20,000/mm^3 (Table 22). A leukocytosis of greater than 20,000/mm^3 is compatible with amoebic liver abscess but should always arouse suspicion of either a primary pyogenic abscess or secondary bacterial infection. Ogden et al (1961) found that the range of leukocyte counts in pyogenic abscess was 3,000 - 80,700/mm^3 with an average of 18,000/mm^3. In amoebic abscess, the maximum was 30,000/mm^3. Eosinophilia is not a feature of amoebic liver abscess.

Table 22

LEUKOCYTOSIS IN HEPATIC ABSCESS

Author	Pyogenic Abscess	Amoebic Abscess
	(percent incidence WCC >20,000/mm^3)	
May et al. (1967)	35	40
Ribaudo and Ochsner (1971)	5	9
Barbour and Juniper (1973)	36	48

Mild to moderate anemia occurs in about half of the patients with hepatic abscess (Table 21). Hemoglobin of less than 8 g/dl is unusual and appears to be related to both the size of the abscess and the duration of symptoms. Studies in amoebic liver abscess indicate an iron reutilization defect as a contributing factor to the anemia. A markedly raised ESR can occur in both pyogenic and amoebic liver abscess, often in association with a polyclonal gammopathy. Prothrombin times have been prolonged in those studies reporting this data. In 3 studies of amoebic abscess, 153 of 256 patients (60%) had prolongation of the PT. Similarly in 6 studies of pyogenic abscess with a total of 183 patients, 112 had an abnormal PT (62%).

BIOCHEMISTRY

Non-specific evidence of liver disease is common in hepatic abscess and there is no recognizable pattern of abnormality. The most consistent, but least specific, finding is hypoalbuminemia and reversal of the A/G ratio. Lamont and Pooler (1958) found a reversed A/G ratio in 190 of 191 patients with amoebic liver abscess but also commented that the finding was almost universal among similar, hospitalized patients in South Africa, without liver abscess. Transaminase elevation is seen in less than half of the patients presenting with amoebic abscess and averages two times normal. In pyogenic abscess, the collected data shows abnormalities of serum transaminases in 50%, compared with 37% for amoebic abscess. This increase may reflect more widespread disease and multiple lesions in pyogenic abscess. Although alkaline phosphatase elevation has been stressed as an indicator of mass lesions in the liver, in the collected data less than two-thirds of patients demonstrated this. In individual series, up to 95% of patients had an abnormal result.

An elevated serum bilirubin was more commonly found with pyogenic abscess in both the collected series and in the comparative studies of May et al. (1967) and Barbour and Juniper (1972). This partly reflects the inclusion of patients with biliary tract obstruction. Gram-negative sepsis can also cause jaundice (see Differential Diagnosis). Bilirubin elevation in amoebic abscess, if present, is modest in most cases, being usually less than 2.5 mg/dl. A high bilirubin in a patient diagnosed as having an amoebic abscess is sufficient to suspect a complicated amoebic abscess, impending hepatic failure, multiple abscesses, obstruction of biliary ducts by a strategically placed abscess or an extremely large abscess (greater than 20 cm) occupying the entire right lobe. BSP retention occurs with and without jaundice and is found in more than 50% of patients, when measured. Transient non-visualization of the gall bladder can also be found in many anicteric patients with liver abscess.

RADIOLOGY

1. Chest X-Ray

The chest x-ray may be abnormal in both pyogenic and amoebic liver abscess (Table 23). The abnormalities are due to either an inflammatory reaction in the diaphragm and pleura overlying the abscess site or to frank rupture of the abscess into the thorax.

The following abnormalities may be seen:

1. Diaphragm - elevation
   - limitation of movement
   - thickening
   - loss of definition

2. Lung - non-specific non-suppurative pneumonitis
   - serous pleural effusion or empyema
   - consolidation and abscess formation

Fluoroscopy of the diaphragm will often demonstrate restricted movement. This may be the result of pleural effusion, pneumoperitoneum, lung reaction or a combination of these. Subdiaphragmatic abscess, as opposed to an intrahepatic abscess, tends to produce greater elevation of the diaphragm and complete immobility. Similar changes on the chest x-ray can be seen in non-infective conditions such as infiltration of the diaphragm by hepatoma extending from the superior surface of the liver. Left lobe abscesses may cause changes (on the left) in the same manner as right lobe abscesses. In addition, a pericardial effusion may be apparent. KUB examination can demonstrate hepatomegaly and, when present, gas in intrahepatic abscesses.

Table 23

CHEST X-RAY ABNORMALITIES IN HEPATIC ABSCESS*

	Number of Patients	Percent (Range)
Amoebic abscess	688/1087	64% (46-75%)
Pyogenic abscess	237/441	54% (20-70%)

*Collected data, 1966-1980.

2. Special X-Ray Techniques

A variety of different methods have been used in attempts to outline the structural defects in the liver resulting from abscess formation. These include:

a) Cholangiography — T-tube, PTC, ERC
b) Infusion tomography
c) Angiography

Pyogenic abscess cavities have been demonstrated by T-tube cholangiogram, percutaneous transhepatic cholangiography and endoscopic retrograde cholangiogram in patients being investigated for obstructive jaundice. In many cases, the patient has died shortly afterwards but whether invasive radiologic techniques were contributory is unclear.

Infusion tomography and total body opacification have been proposed as methods of outlining hepatic abscesses. With these techniques, the abscess cavity, because of its avascular nature, has a decreased amount of contrast agent associated with it. In addition, the edge of the cavity sometimes demonstrates increased uptake of contrast material. This technique has not been used in many patients and is accuracy is unknown.

In the investigation of a solitary mass lesion of the liver, angiography may be used to differentiate a vascular lesion such as hepatoma or hemangioma from an avascular cyst or abscess. The findings on angiography are dependent on the size, multiplicity and chronicity of the abscess(es). The technique is invasive and may be misleading in tumors with necrotic centers. In one study by Viana et al. (1974) of 20 patients with proven amoebic liver abscess, arteriography correctly identified 15.

NUCLEAR MEDICINE

Liver scanning with various types of isotopes has been used for more than 15 years in many centers. The entire liver is easily imaged and the technique has proven to be of great value as a screening test for hepatic abscess, although not as accurate as the 100% originally claimed. The isotopes which have been routinely used include ^{131}I rose bengal, ^{198} Au colloidal gold, ^{113m}In coprecipitates and ^{99m}TC sulphur colloid. Special isotope studies can also be done using ^{67}Ga citrate and blood pool labels.

LIVER SCAN TECHNIQUES

1. Radiopharmaceuticals metabolized by liver - ^{131}I rose bengal, ^{99}Mo, $^{69m}ZnCl$

2. Colloid substances cleared by RE system - ^{198}Au, ^{99m}Tc, ^{113m} In

3. Scintiangiography (blood pool label) - ^{99}Tc-HSA, $^{113m}InCl_3$, ^{113m}In transferrin

4. Neoplasm and Abscess label - ^{67}Ga citrate

In a large study of 3,379 patients, Cuarón et al. (1970) found that these radioactive compounds were equally accurate in diagnosis. In general, ^{99m}Tc sulphur colloid is used because of its low radiation dose and pure gamma emission. Colloids are taken up by the reticuloendothelial cells of the liver and the extraction efficiency probably depends on the size of the particle. Usually 85% is cleared by the liver, 5% by the spleen and 5-10% by the remaining RE cells. Mass lesions can be detected by a decrease in uptake when they are >2 cm in diameter. Smaller lesions, particularly if deep within the substance of the liver, cannot be detected. Problems in demonstration or interpretation of defects on liver scan can occur for a variety of reasons. These include:

1. Normal anatomic variations - porta hepatis, gallbladder fossa
2. Dilated ducts
3. Focal defects in diffuse disease
4. Extrahepatic structures - subphrenic and subhepatic abscesses
   - retroperitoneal masses
   - pleural effusion

Liver scans using a variety of isotopes have demonstrated defects in 50-100% of patients with hepatic abscess (Table 24). Abscesses may not be detected when they are small or on the lateral surface of the liver.

In some instances, as reported by Kew et al. (1979), misinterpretation can occur because of the presence of splenomegaly and shunting of radionuclide to bone marrow in an infectious process.

Table 24

LIVER SCAN ABNORMALITIES IN HEPATIC ABSCESS*

	Number of Patients	Percent (Range)
Amoebic abscess	423/435	97 (84-100)
Pyogenic abscess	182/216	84 (50-100)

*Collected data, 1966-1980.

Colloid liver scans are non-specific, they do not differentiate between the causes of focal defects. Attempts have been made to improve diagnostic capabilities with additional radionuclides. In particular, scintiangiography using a blood pool label and gallium scintigraphy may be useful. The blood pool scan allows differentiation of hemangiomas and vascular hepatomas, however all abscesses and cysts as well as some tumors are avascular. Dynamic scintigraphy (flow studies) using colloid radionuclide can also give additional information regarding the vascularity of focal lesions.

Table 25

SCHEME FOR DIFFERENTIATION OF HEPATIC MASSES*

Lesion	^{99m}Tc sulphur colloid	^{99m}TC-HSA	^{67}Ga citrate
Abscess	+	-	+
Cyst	+	-	-
Tumor 1°	+	+	+
2°	+	+	±

*Adapted from Müller-Brand et al. (1977).

Gallium concentrates in lysosome-like organelles in leukocytes and neoplastic cells. Therefore, hepatic lesions such as hepatoma and pyogenic abscess demonstrate areas of increased uptake when scanned with ^{67}Ga citrate (Table 25). Amoebic abscesses, on the contrary, have only a rim of increased uptake with a central defect. The use of a computerized substraction technique

and sequential scanning with ^{99m}Tc and ^{67}Ga can be useful in giving added definition to the ^{67}Ga citrate image. The major problem is that both pyogenic abscesses and metastatic tumors have been reported to have ^{67}Ga scan defects similar to those of amoebic abscesses. The combined use of a colloid scan, blood pool scan and ^{67}Ga citrate study has been proposed for focal defects (Table 25). However, since each technique has both false positive and false negative results, the benefit may be insufficient to justify the additional expense and radiation exposure.

ULTRASONOGRAPHY

The development of grey-scale ultrasonography has allowed more accurate diagnosis of hepatic abscesses in recent years. Ultrasound techniques can be used to identify focal defects in the liver and have the advantage of differentiating cystic from solid structures. The major disadvantages are:

a) Requirement for considerable technical expertise
b) Inability to pass through air (bowel gas, lung) or bone (thoracic cage)
c) Image greatly affected by type of equipment.

Intrahepatic cysts are differentiated by sharp, clear margins and an echo-free center. Abscesses, necrotic tumor and resolving hematomas of the liver have irregular margins, varying numbers of echoes centrally and a distinctive peripheral echo pattern. Experts may be able to distinguish between various images. Solid lesions such as tumors may have well-defined or poorly defined borders depending on the amount of peripheral infiltration; the center of a solid lesion may contain multiple irregular echoes. The detection of localized lesions depends on:

a) size of lesion
b) location within the liver
c) conscientiousness of operator
d) shape of the patient

The ability of ultrasonography to detect amoebic liver abscesses has been assessed by Boultbee et al. (1979). They correctly identified 95% of cases and had low false positive (10%) and false negative (15%) rates (Table 26). The abscess walls were irregular in 32% and the centers of the lesions had decreased echoes (by 2/3 or more) in 93%. Observer error and poor technique were the main factors in misdiagnosis.

Table 26

ULTRASONOGRAPHY IN AMOEBIC ABSCESS*

Diagnosis	Ultrasound	# Patients	Incidence
Amoebic abscess	correct	151/159	0.95
	incorrect	8/159	0.05
Other	correct	85/94	0.90
	incorrect	9/94	0.10

*From Boultbee et al. (1979)

False negative 0.05, false positive 0.10

Two recent U.S. studies, one by Ralls et al. (1979) and the other by Landay and colleagues (1980) have reported on ultrasonography in amoebic abscess. In both studies many of the abscesses were contiguous with the capsule. Landay et al. (1980) have also documented changes in ultrasound findings with progression and resolution of the abscesses. Early changes in pyogenic abscesses which have been described by Freeny (1980) and Dewbury et al. (1980) include focal areas of high level echoes, a peripheral echo-free halo, distal acoustic enhancement and progressive change over a short time. Pyogenic and amoebic abscesses are similar at ultrasound examination. Ultrasound localization can aid in aspiration of abscesses.

COMPUTED TOMOGRAPHY

Computed tomographic scanning can detect hepatic abscesses but its value over other, less-expensive methods, is under review. Abscesses are less dense than the surrounding liver and can therefore be demonstrated (CT will not differentiate between structures of equal density). Cysts and abscesses can be confused. The presence of intrahepatic gas in an abscess, even in small amounts, will help in differentiation. The injection of intravenous contrast will aid in detecting abscesses which are of a density similar to normal liver, by enhancing the tissue immediately surrounding the abscess. Diagnostic difficulties can arise with intrahepatic neoplasms which are often less dense than normal liver, particularly when the centers are necrotic. CT is less accurate in diffuse liver disease than it is in focal liver disease. A recent study by Scherer et al. (1978) assessed the diagnostic accuracy of CT in focal hepatic disease in 45 patients and 60 normals (Table 27). The studies were read routinely and in retrospect without awareness of the clinical diagnosis. Two patients had abscesses both of which were correctly diagnosed.

Table 27

DIAGNOSTIC ACCURACY OF CT IN CIRCUMSCRIPT LIVER DISEASE*

	Routine Interpretation		Retrospective
	Number	Incidence	Incidence
True positive	38/45	0.84	0.89
True negative	47/60	0.78	0.90
False positive	13/60	0.22	0.10
False negative	7/45	0.16	0.11

*From Scherer et al. (1978).

Rubinson et al. (1980) have recently compared the diagnostic accuracy of CT with scanning and ultrasonography, in the detection of intrahepatic abscesses (Table 28). They analyzed studies in 17 patients with proven abscesses (12 pyogenic and 5 amoebic). Routine ^{99m}Tc sulphur colloid scanning failed to detect multiple small abscesses in one patient and observers incorrectly interpreted another defect as an anatomic variant (renal fossa). ^{67}Ga citrate scanning was negative in a patient who had received antibiotic treatment for 24 hours prior to injection. An additional patient was taken to surgery after a negative 6 hour ^{67}Ga scan and not included in the results.

Table 28

COMPARISON OF IMAGING STUDIES IN HEPATIC ABSCESS*

Study		Incidence
CT	15/17	0.88
Ultrasonography	12/16	0.75
Colloid scan	14/16	0.88
Gallium scan	9/10	0.90

*From Rubinson et al. (1980).

Ultrasonography did not detect the multiple small abscesses associated with a dilated biliary tree which was also missed by scanning and CT. One abscess high in the dome of the liver was missed on ultrasound and another abscess in a fatty liver was not demonstrated. In an additional patient, the gall bladder was examined and a liver abscess missed, although it was present in retrospect. CT misdiagnosed the fatty liver plus abscess and the small multiple abscesses. This study shows similar diagnostic accuracy with all methods of imaging hepatic abscesses. Unfortunately, false positive results (in patients who were suspected of having abscesses but on final diagnosis did not) were not presented.

MICROBIOLOGY OF PYOGENIC ABSCESS

The causative organisms in pyogenic liver abscess may be isolated from the abscess contents and from blood. Positive results have been reported more often from cultures of abscess material. Multiple organisms are found in a variable number of the cultures and no growth in as many as 20%. Inadequate anaerobic culturing techniques are often the cause of sterile cultures. The incidence of infection with multiple organisms has increased since the widespread usage of antibiotics. In a recent collected series (McDonald and Howard, 1980), data were available on 604 of 1085 patients reviewed (Table 29). Enteric organisms, particularly Escherichia coli (37%), Proteus (13%) and Klebsiella-Enterobacter (12%) were most often cultured. This reflects the intra-abdominal origin of most infections. Staphylococci were found in 23% of patients and were associated with hematogenous spread. De la Maza et al. (1974) reported that Staphylococcus and E.coli were commonly encountered organisms in pure cultures (23 patients) while mixed infections (26 patients) were characterized by a high prevalence of gram-negative bacilli and enteric gram-positive cocci.

Table 29

Microbiology in 604 patients with pyogenic hepatic abscesses.

	Number	Percent
Escherichia coli	221/604	37
Staphylococcus aureus	141/604	23
Proteus	80/604	13
Klebsiella-Enterobacter	74/604	12
Enterococcus	62/604	10
No growth	45/604	7
Streptococcus viridans	44/604	7
Anaerobes (*Bacteroides* species, *Peptostreptococcus, Clostridium* species)	36/604	6
Pseudomonas	35/604	13
Others (*Serratia, Providencia, Salmonella,* Beta-hemolytic *Streptococcus, Actinomyces, Nocardia,* Unclassified *Streptococcus*)		

From McDonald and Howard (1980)

"Sterile" abscesses were found in 7% of patients in the collected series. In individual series since 1966, there has been no growth in up to 29% of cultures. This may reflect incompleteness of collection, inadequate anaerobic culturing techniques or antibiotic therapy before culture. Anaerobic bacteria were cultured in only 6% of the collected cases. Sabbaj et al. (1972) have reviewed the importance of anaerobic infections as the cause of liver abscess. They were able to find 210 anaerobic isolates from at least 165 cases of liver abscess. There were multiple abscess in 72 patients of their collected series and solitary abscesses in 53 (40 unknown). In their own series of 51 liver abscesses, 45% were due, in whole or in part, to anaerobic infections. Pitt and Zuidema (1975) reported a significant increase in the prevalence of anaerobic infections (16→36%) from 1952-1962 to 1962-1972. They also found a decreased mortality in patients with pure anaerobic or mixed infections; these were associated with a higher incidence of solitary abscess, which has a better prognosis. No potential source of infection was identified in a number of patients with solitary anaerobic liver abscess in this series and in those of Sabbaj et al. (1972), Lee and Block (1972) and Lazarchick et al. (1973). There may be, therefore, a clinical subgroup of anaerobic liver abscesses which are frequently solitary with a single infecting organism and no discernible etiology. The prognosis in this group of patients is favorable. Sabbaj et al. (1972) reported no deaths in 14 patients who were diagnosed antemortem. In the 5 years from 1975 through 1979, there have been at least 3 similar cases at PMH with pure or mixed anaerobic infection and cryptogenic liver abscess. Anaerobic infection of hepatic metastases has been proposed by Trump et al. (1978) as the mechanism of fever production in patients with metastatic liver disease. They reviewed 4 cases of abscess complicating malignant deposits in the liver and all were due to anaerobic infection. Secondary infection of amoebic abscesses is usually due to enteric flora. Other

rarer causes of pyogenic liver abscess which have been reported include Yersinia enterocolitica, Edwardsiella tarda (enterobacteriaceae) and aeromonas hydrophila. Thirteen cases of generalized Yersinia infection have been reported by Rabson et al. (1975). In 6 patients, all of whom had cirrhosis, a subacute, localizing infection occurred. This was characterized by malaise, fever, hepatomegaly and abdominal pain. Autopsies were performed in 3 of the 5 who died and liver and spleen abscesses were found in all.

MICROSCOPY AND SEROLOGY IN AMOEBIC ABSCESS

The diagnosis of amoebic liver abscess is not dependent on stool examination for E.histolytica. The finding of cysts or trophozoites in the stool merely supports a clinical diagnosis of amoebic abscess (Table 30). Overdiagnosis of E. histolytica (false positive) most frequently occurs because leukocytes are not identified by staining of specimens. Underdiagnosis occurs if the specimens are incorrectly handled, technicians lack expertise or E.histolytica are not present because of interfering substances (Table 31).

Table 30

INTESTINAL AMOEBIASIS AND AMOEBIC ABSCESS*

Finding	# Patients	Percent (Range)
Diarrhea	233/1205	19% (7-47%)
Stool positive	87/626	14% (0-75%)

*Collected series (1966-1980).

Table 31

Substances That Interfere with Stool Examination for Parasites.*

ANTIBIOTICS	ENEMAS
Tetracyclines	Hypertonic salt
Sulfonamides	Soap
ANTIPARASITIC DRUGS*	Tap water
Antiprotozoal agents	ANTIDIARRHEAL PREPARATIONS
LAXATIVES, ANTACIDS	Bismuth
Castor oil	Kaolin compounds
Magnesium hydroxide	
RADIOLOGIC CONTRAST MEDIUM	
Barium sulfate	

From Krogstad, Spencer and Healy (1978)

Aspirates of amoebic abscess contents contain trophozoites in almost all cases when the last few milliliters of fluid are examined by experienced personnel, since amoebae are usually present in the periphery of the abscess. Gram-stain and culture for aerobic and anaerobic bacteria should also be done routinely on aspirates. Aspiration for diagnosis alone is seldom necessary since serological tests give sufficient evidence of etiology in the majority of patients with amoebic liver abscess. There are a number of different serologic assays for detection of antibodies in patients with amoebiasis (Table 32). Early tests had very high false positive rates because the antigen was obtained from E.histolytica cultured with Clostridia, Trypanosoma cruzi or Mycoplasma. After the development of a technique to culture the amoebae alone, many of these problems were solved.

Table 32

SEROLOGIC TECHNIQUES USED IN AMOEBIASIS

	True +	False +
1. Indirect hemagglutination (IHA)	90-95%	0-5%
2. Latex agglutination (LA)	98%	0-15%
3. Gel diffusion precipitin (GDP)	85-95%	0-15%
4. Counterimmunoelectrophoresis (CIEP)	>90%	0-10%

The indirect hemagglutination (IHA) and latex agglutination (LA) tests demonstrate very good correlation when compared and appear to be detecting the same antibody. A different antibody class (precipitating rather than agglutinating) is detected by gel diffusion (GDP) and counterimmunoelectrophoresis (CIEP). Less commonly used serologic techniques include cellulose acetate diffusion, complement fixation, immunofluorescent antibody and E.L.I.S.A. They also correlate mainly with CIEP and GDP results and thus appear to detect the precipitating antibody.

1. Indirect hemagglutination (IHA) is one of the most sensitive of the serologic tests available. 90-95% of patients with amoebic liver abscesses have positive titers (at least 1:128) and a majority have titers greater than 1:512. Positive results are also obtained in patients with amoebic colitis alone and in some patients with a remote past history of amoebiasis (Table 33). The detected antibody persists in the serum and this may be the cause for apparent false positive results, which are higher in countries where amoebiasis is more prevalent.

Table 33

IHA IN AMOEBIASIS*

Origin of Sera	# Patients	% Positive
Amoebic abscess	117/121	96
Amoebic colitis	68/83	82
Asymptomatic cyst passage	6/70	9
Liver disease	1/31	3
Parasitic disease	0/200	0
Hospitalized patients, U.S.	5/556	0.9
Normal (Alaska, Greenland)	0/207	0

*From Milgram et al. (1966)

The major disadvantage of the IHA is that single specimen testing is not possible. In the past, the assay was also slow, with a minimum of 48 hours being required. Newer methods have shortened the assay and results are now available within a few hours. The Center for Disease Control in Atlanta, Georgia and the State Health Department provide IHA testing for amoebiasis and since July 1980 the Clinical Immunology/Serology Laboratory at Parkland Memorial Hospital have been using the IHA as a confirmatory test after latex agglutination.

2. Latex agglutination (LA) is a simple, rapid, slide test which is complete in minutes. The latex is sensitized with antigen prepared from axenically cultured E.histolytica. Most results can be read by naked eye examination, occasionally microscopic examination is required. It is a reliable screening test which does not require experienced personnel and gives very few false negative results (Table 34). If amoebiasis is endemic, the number of positive results without liver abscess is high because the antibody, like that detected in IHA, remains for varying lengths of time. In a study by Manse et al. (1972) positive results in control sera were as high as 18.5% but no false negatives were found. The LA test ("Serameba") is used as a screening test at PMH and positive results are checked by IHA.

Table 34

LATEX AGGLUTINATION TEST IN AMOEBIASIS*

Patient population	Number Positive
Amoebic liver abscess	98/100
Amoebic disentery	96/100
General medical patient (South Africa)	15/100
Blood donors - European	0/100
- Non-European	5/100

*From Morris et al. (1970)

3. Gel diffusion precipitin tests (GDP) are suitable for single specimen testing. Maddison, Powell and coworkers (1965) found that the test is positive in 85-95% of patients with invasive amoebiasis (intestinal or hepatic) with up to 20% false positive results in patients hospitalized for conditions other than amoebiasis. Normal blood donors residing in an endemic area also had up to 10% false positive results. An initial negative result which converts to positive within a few days can occur in patients who present early with acute disease.

4. Counterimmunoelectrophoresis (CIEP) is positive in more than 90% of sera from patients with extraintestinal amoebiasis. The test may distinguish between patients with active disease and those with previous infection by the presence of multiple band patterns.

The cellulose acetate diffusion test has the advantage of being able to use stored test material. Complement fixation (CF) is less sensitive and is invalidated by anticomplementary serum. Immunofluorescent antibody (IF) tests have been reported to be very sensitive, with positive results in almost all patients with amoebic abscess, but it is less specific than GDP and CIEP. Recently Yang and Kennedy (1979) have described an E.L.I.S.A. for amoebiasis which gave positive results in all 53 sera from patients with amoebic liver abscess and had less than 5% false positives in more than 1000 control sera. It is important to remember that false negative results may occur as with any test and that an early negative test may convert to positive in a few days (Table 35).

Table 35

SEROLOGIC RESULTS

Days after hospitalization	CIEP	SAFA	FIAX	IHA
2	−	< 1:8	ND	< 1:64
3	−	< 1:8	+	< 1:64*
4	−	< 1:8	ND	1:128
9	+	1:64	ND	1:256*
13	+	1:64	+	1:512
20	+	1:64	ND	1:256
140	−	< 1:8	−	< 1:64

From Stevens et al. (1979)

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of hepatic abscess includes hepatic disease other than abscess, intra-abdominal infection or inflammation and hepatic manifestations of non-hepatic infections. In addition, hepatic abscesses with complications, due to extension of the process beyond the liver, may present as pulmonary or pericardial disease.

1. Hepatic disease other than abscess

a) Primary or secondary malignancy
b) Cirrhosis + infection
c) Hepatitis: viral, bacterial, alcoholic
d) Cyst: hydatid, simple or polycystic congenital
e) Hematoma
f) Recurrent pyogenic cholangitis + abscess
g) Perihepatitis: gonococci, chlamydia

Hepatoma can be the most difficult disease to distinguish from hepatic abscess. This is particularly true in South Africa and South East Asia where the incidence of hepatoma is much higher than in the U.S. Cysts and hematomas of the liver can become secondarily infected, thus confusing the clinical presentation. Recurrent pyogenic cholangitis occurs in Chinese both in South East Asia and after migration to the U.S. Pyogenic abscesses occur during the course of the disease but may not be present with every episode of fever, abdominal pain and tenderness. This disease is characterized by the presence of biliary calculi or biliary sludge in the intrahepatic ducts.

2. Hepatic manifestations of non-hepatic infection

a) Jaundice in bacterial pneumonia
b) Jaundice in gram-negative bacterial infection

The occurrence of jaundice in bacterial pneumonia has not been reported from Europe or the U.S. Since 1950, all the recent reports have been from Africa and the Pacific. Studies have demonstrated that the jaundice is not due to hypoxia, fever or G-6-PD deficiency. Interestingly, in the studies giving information regarding sex and race, 85-100% are male and 90-100% are black (Table 36).

Table 36

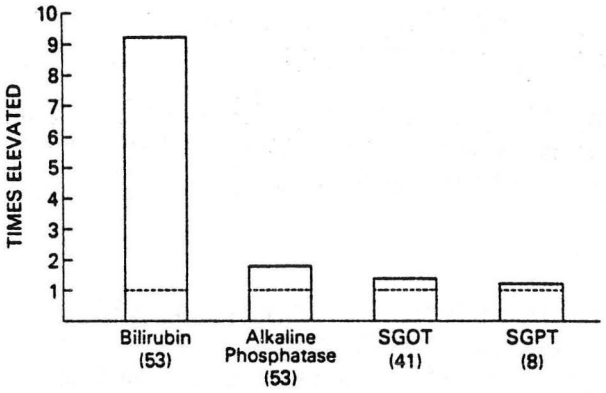
Reported Prevalence of Jaundice in Patients with Lobar Pneumonia

Author (Year)	Ref.	Frequency	Sex distribution	Racial distribution	Geographical area
King, cited by Klemperer (1933)	47	6.6%	NS	NS	USA
Rosenbluth and Block (1937)	48	23.5%	90% M	NS	USA
Curphey and Soloman (1938)	49	29.9%	NS	NS	USA
Gelfand and Lewis (1942)	52	18.0%	NS	100% B	Rhodesia
Turner et al. (1943)	50	67.7%	100% M	100% B	USA
Zimmerman and Thomas (1950)	51	13.9%	90% M	90% B	USA
Radford et al. (1967)	61	46.6%	85% M	100% P & NG	Papua & New Guinea
Tugswell and Williams (1977)	60	22.4%	100 M	100% B	Nigeria
Hall and Parry (1963)	53	11 cases	91 M	100% B	Nigeria
Kibukamosoke et al. (1964)	54	21 cases	100% M	100% B	Uganda
Clain and Gelfand (1967)	*55	8 cases	100% M	100% B	Rhodesia
Mekel et al. (1966)	56	41 cases	95% M	100% B	S. Africa

NS = not stated; M = male; B = black; P & NG = Papua & New Guinea.

Jaundice in gram-negative sepsis is most often seen in infants but occasionally occurs in adults. The bilirubin is elevated when transaminases are normal or near normal (Fig XI). In one study, vitamin B_{12} levels were also normal, again suggesting lack of parenchymal cell destruction. The combination of jaundice and gram-negative bacterial infection has a grave prognosis with 90% mortality.

Figure XI



Mean height of serum bilirubin, alkaline phosphatase serum glutamic oxaloacetic transaminase (SGOT), and serum glutamic pyruvate transaminase (SGPT) in 53 cases of jaundice associated with sepsis from six recent reports.[2,3,5,14–16,37] The total number of cases for which each test was reported is given in parenthesis. (Modified from Miller et al., reference 2).

From Zimmerman et al. (1979)

3. Intra-abdominal infection or inflammation

a) Subphrenic, subhepatic and perinephric abscess
b) Ascending cholangitis, cholelithiasis, cholecystitis, infected mucocoele of gallbladder
c) Acute pancreatitis, pancreatic pseudocyst
d) Acute appendicitis, typhoid fever, intestinal obstruction, intestinal perforation
e) Peptic ulcer + perforation

Investigations which demonstrate a structural defect in the liver are of great importance in the differentiation of other intra-abdominal pathology and diagnosing primary hepatic abscesses, when the presentation is one of pulmonary or pericardial disease.

TREATMENT AND PROGNOSIS

Undiagnosed, hepatic abscess is almost invariably fatal. New methods of investigation, if applied, can allow early diagnosis and improve the prognosis. Once diagnosed, amoebic liver abscesses are treated with amoebicidal drugs and, if required (see below), aspiration or formal surgical drainage. In pyogenic abscess, appropriate antibiotic therapy is generally augmented by surgical drainage. Recent reports suggest that aspiration or percutaneous drainage may be alternative forms of therapy.

MEDICAL THERAPY: Amoebic Abscess

Medical therapy for amoebic liver abscess requires either a single agent or combination of agents which will effectively eliminate both intestinal and extra-intestinal amoebae.

a) Emetine hydrochloride

Emetine HCl was introduced by Rogers in 1912, replacing ipecacuanha which had long been used in treatment. It is an efficient tissue amoebicide but frequently fails to eradicate luminal amboebae and this may lead to apparent treatment failures (Table 37). The preparation is given parenterally and until the recent introduction of intravenous metronidazole, it was being used when oral preparations were contra-indicated or of questionable efficacy due to lack of absorption. An oral preparation, emetine bismuth iodide, has yielded high cure rates in intestinal amoebiasis but gastrointestinal side effects are a major disadvantage. Dehydroemetine was introduced in 1959 as a less toxic alternative to emetine HCl but on further evaluation probably has toxicity and activity equal to emetine. It is only available from the C.D.C. The use of emetine HCl or dehydroemetine requires hospitalization and cardiac monitoring. In large or cumulative doses cardiac failure may result from focal necrosis of cardiac muscle. Both agents are given in a dose of 1.0 - 1.5 mg/kg/day intramuscularly or by deep subcutaneous injection for up to 10 days.

Table 37

RESULTS OF AMEBIC LIVER ABSCESS TREATMENT

Therapy[a]	Percentage cure
Emetine HCl (65 mg × 10 days)	88
Emetine HCl (65 mg × 2 courses)	100
Dehydroemetine (80 mg × 10 days)	88
Dehydroemetine (80 mg × 2 courses)	89
Chloroquine (× 28 days)	71
Emetine (65 mg) + chloroquine	98
Dehydroemetine (80 mg) + chloroquine	100

[a] In all instances a luminal amebicide was also given and when concomitant dysentery was present tetracycline was added.

From Powell (1972)

b) Chloroquine phosphate

The effectiveness of chloroquin phosphate in amoebic liver abscess was first reported by Conan in 1948. It is effective against amoebae residing in tissue and is concentrated up to 500 times in the liver. It has little activity against intestinal amoebae and must be given in conjunction with a luminal amoebicide. Prolonged courses are required for a response rate equal to that of emetine HCl, however important side-effects are less common. It may cause mild headache, itching, incoordination, peripheral neuropathy, seizures, diarrhea and ECG changes in a small number of patients. With long term administration there have been reports of retinopathy and deafness has been described in children of mothers who have taken chloroquine during pregnancy. The usual dosage regimen is 500 mg twice daily for one or two days followed by 500 mg daily for up to 10 weeks. Such prolonged treatment necessitates a compliant patient population. When given in a shorter course in conjunction with emetine or dehydroemetine, it is extremely effective (Table 37,38).

Table 38

RESULTS OF MEDICAL THERAPY OF AMOEBIC ABSCESS*

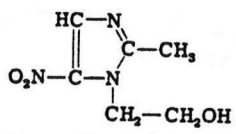
Therapy	Dose	Percentage Cure
Emetine HCl	1 mg/kg/d x 10 d	90
Dehydroemetine	1 mg/kg/d x 10 d	88
oral preparation		45
Chloroquine phosphate	150 mg b.d. x 20 d	75
Emetine/Dehydroemetine	as above	
+ Chloroquine	as above	100

*From Vakil and Dalal (1974)

c) Metronidazole

Metronidazole was introduced in 1959 for the treatment of trichomonas and was also found to be useful in giardiasis. It's value in amoebiasis was not realized until 1966. It is a nitro-imidazole derivative.

Figure XII



Metronidazole: 1-(2hydroxyethyl)-2-methyl-5-nitromidazole

The oral preparation is well absorbed and has a half life of >8 hours. Peak blood levels are similar after oral or intravenous administration. It diffuses well into tissues, little is bound to protein and it is excreted in urine. The mechanism of action of the drug is by interaction with low redox potential election transport proteins and subsequent reduction of the nitro group on the drug. Intermediate products kill by an unknown mechanism. There is little suppression of indigenous colonic flora because of degradative reduction in the anaerobic environment of the colon. There may be significant effects in patients with diarrhea, in patients having certain other antimicrobial agents and in patients on high dosage, when the normal colonic environment is altered. Metronidazole is effective against amoebic liver abscess in over 90% of patients when doses of 750 mg three times a day are used (Table 39). The duration of therapy is somewhat unclear but should continue for at least 10 days. Because of reports of relapse, some authorities administer this agent for up to three weeks.

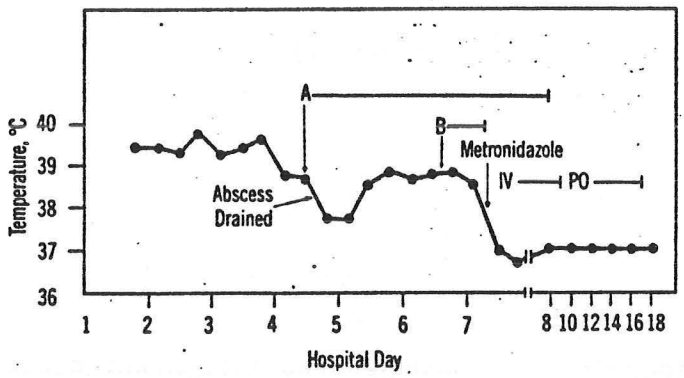
Table 39

METRONIDAZOLE FOR AMOEBIC LIVER ABSCESS

Author	Oral Dosage Regimen	% cured
Powell (1972)	2.4 g - 24 g total 1 to 10 days	98
Vakil and Dalal (1974)	400 mg t.i.d. x 10 d	95
Everett (1974)	750 mg t.i.d. x 5-25 d	100
Cohen et al. (1975)	750 mg t.i.d. x 10 d	94

Intravenous metronidazole has been used for patients when oral preparations are contraindicated and excellent results have been reported (Fig XIII). It is useful in patients having complications requiring surgical drainage. Metronidazole should not be used in a therapeutic trial for diagnosis since anaerobic infections, either pure or mixed, can respond initially. Chloroquine with or without emetine is preferable.

Figure XIII



Temperature chart. Defervescence occurred four hours after starting parenteral administration of metronidazole. A represents tobramycin sulfate, ampicillin sodium, and clindamycin phosphate; B, chloroquine phosphate; IV, intravenously; and PO, orally.

From Kovaleski et al. (1981)

Cohen et al. (1975) in a prospective randomized trial compared the efficacy of metronidazole 750 mg t.i.d. x 10 days to chloroquine phosphate (standard dose 500 mg q.d. x 10 weeks). They entered 36 patients in the trial and an additional 30 patients who were not randomized were also followed in parallel.

Table 40

TRIAL OF METRONIDAZOLE VS. CHLOROQUIN IN AMOEBIC LIVER ABSCESS

Patient Population	Chloroquine	Metronidazole
	no. cured/no. treated	
Randomized	19/20	15/16
Non-randomized	8/8	19/20

From Cohen et al. (1975).

The single treatment failure with chloroquine was cured with metronidazole. One treatment failure with metronidazole responded to a second course, the other was cured with chloroquine. The response was somewhat more rapid with metronidazole, with improvement occurring in 2.3 days, compared with an average of 2.6 days with chloroquine. Larger abscesses took a longer time to respond and all treatment failures were in this group. During the study, 2 patients received multiple concomitant drug therapy because of the severity of their illness and both died.

Possible treatment failures with metronidazole have been anecdotally reported. Except for Weber (1971) and Wilde (1973), these have been individual cases. In many, there is either the possibility of reinfection or of failure to eradicate all intestinal cysts. Powell (1972) reported that 71 of 72 patients with amoebic liver abscess were cured after metronidazole therapy but 13 continued to pass cysts. In other instances, metronidazole may fail to cure the initial clinical presentation. In general, such patients will respond to institution of an additional course of metronidazole or an alternative drug. Similar findings occur with emetine and chloroquine therapy. Some patients may require aspiration and/or drainage, particularly if the abscess is large (see also surgical therapy below). Alternatively there may be inadequate tissue penetration or a primary defect in the host response. Eventual cure in most cases makes this latter explanation unlikely.

Table 41

Percentage incidence of side effects of drugs

	Drug		
Side effect	Emetine	Chloroquine	Metronidazole
Nausea	6.2	7.1	7.4
Vomiting	5.6	6.1	5.7
Anorexia	0	4.6	0
Weakness	3.4	5.3	0
Glossitis	0	0	1.5
Psychosis	0	0	1.5
Tremor	0	0	0.7
Muscle spasm	0	0	0.7

From Tsai (1973)

Minor side effects of metronidazole therapy include reversible neutropenia, gastrointestinal disturbances, metallic taste, urticaria, ataxia, vertigo, headache and peripheral neuropathy. Similar side effects occur with both emetine and chloroquine (Table 41). In conjunction with alcohol, metronidazole has a disulfiram-like reaction ("Antabuse"). It also inhibits the metabolism of warfarin. Potential major side effects are mutagenicity and tumorigenicity. Reduction of the nitro group is essential for both the anti-bacterial and mutagenic activities. Mutagenicity was demonstrated in the Ames Salmonella mutant system. Some rodent studies (mouse and rat) have found increases in pulmonary and mammary tumors, others in the hamster have been negative. In one rat study, the drug-treated rats lived longer, although there was an increase in the number of tumors. Human studies have not shown a carcinogenic effect although interestingly a retrospective study of 771 women given metronidazole for trichomonas found an increase in lung cancer. There were 4 cases (expected 0.6), all in smokers, but the increase was not statistically significant. Because of the possibility of mutagenicity and carcinogenicity, the use of metronidazole should be reserved for clearly indicated circumstances.

d) Other tissue amoebicides

Niridazole (Ambilhar®) and aminosidin have both been used, either alone or in combination with other drugs, for the treatment of amoebic abscess. They have no benefits over the previously reported drugs. Similarly, Tinidazole, a new nitro-imidazole derivative, is safe and effective but is no better than metronidazole and has the same side effects.

e) Luminal amoebicides

Therapy must be combined with an intraluminal amoebicide if chloroquine and emetine or dehydroemetine are used and if passage of cysts persists after metronidazole therapy. The C.D.C. recommends diloxanide furoate (Furamide®) 500 mg t.i.d. x 10 days. The compound is safe and well tolerated with occasional gastrointestinal side effects. It is active against E.histolytica only in the presence of bacteria. It is only obtainable through the C.D.C. Diiodohydroxyquin (Diodoquin®) is the available alternative therapy. Optic atrophy and blindness have been reported after prolonged use; rashes, gastrointestinal upset and thyroid enlargement have been described as well. The usual dose is 650 mg t.i.d. x 20 days. The current C.D.C. recommendations for intestinal and extraintestinal amoebiasis are summarized in Table 42.

Table 42

Treatment of Amebiasis.

Form of Infection	Dosage*
Intestinal:	
Cysts on stool examination:	
Diloxanide furoate (Furamide)†	500 mg 3 times/day × 10 days
Di-iodohydroxyquin	650 mg 3 times/day × 20 days
Metronidazole (Flagyl)	750 mg 3 times/day × 5–10 days
Trophozoites on stool examination:	
Metronidazole (Flagyl)	750 mg 3 times/day × 5–10 days
Dehydroemetine†	1.0–1.5 mg/kg daily intramuscularly or subcutaneously × 10 days
Extraintestinal:	
Metronidazole (Flagyl)	750 mg 3 times/day × 5–10 days
Chloroquine plus	500 mg daily × 10 wk
di-iodohydroxyquin[10]	650 mg 3 times/day × 20 days
Dehydroemetine† plus	As above
chloroquine	500 mg/day × 2–3 wk
Dehydroemetine†	As above

*Doses listed are those suggested for adults. Unless otherwise indicated, drugs are taken by mouth.

†Investigational drug available through the Parasitic Disease Drug Service, Center for Disease Control ([404] 633-3311, nights & weekends 633-2176).

From Krogstad, Spencer and Healy (1978)

SURGICAL THERAPY: Amoebic Abscess

In some areas of the world, needle aspiration of hepatic amoebic abscesses is routinely performed with medical therapy. The occurrence of treatment failures with metronidazole was thought to reflect the lack of routine aspiration in the U.S. even though other causes of treatment failure were present. Present opinion is that medical therapy is adequate, especially in patients who are not toxic or distressed.

Indications for needle aspiration or surgical drainage are as follows:

a) Lack of response to medical therapy
b) Impending rupture
c) Left lobe abscess
d) Diagnosis
e) Complications

When there is no response to appropriate medical therapy after 48-72 hours, needle aspiration will confirm the diagnosis and exclude pyogenic abscess or secondary infection of an amoebic abscess. Aspiration has not been shown to hasten resolution time. In a collected series of 515 patients, aspiration did not increase mortality (Table 43). A number of authors have emphasized the need for scrupulous aseptic technique during closed aspiration of amoebic abscesses, principally to avoid secondary infection. With the advent of ultrasonographic and CT guidance, the advantages of accurate localization need to be weighed against the likelihood of infectious complications following aspiration outside an

operating room. In experienced hands, complications of aspiration are rare. Dorrough (1967) reviewed 2,251 clinical cases and found no reports of hemorrhage and only 7 of leakage from the puncture site. Secondary infection can occur in up to 8%.

Table 43

THERAPEUTIC RESPONSE IN AMOEBIC ABSCESS

Therapy	Number of Patients (Percentage)	Deaths (Percentage)
Nil (undiagnosed)	9 (1.8)	9 (100)
Medical only	151 (29.3)	7 (4.6)
Medical + aspiration	168 (32.6)	3 (1.8)
Medical + drainage	187 (36.3)	15 (8.0)
Total	515	34 (6.6)

Impending rupture as evidenced by increasing pleural or peritoneal reaction, progressive diaphragmatic elevation and increasing liver tenderness and enlargement should be treated by evacuation of the abscess. Most investigators feel that patients with left lobe abscesses should have early drainage procedures performed, rather than aspiration, in order to avoid extension into the pericardial space (see also clinical features section on pericarditis). Open surgical drainage is indicated for patients with rupture into the peritoneal cavity. Conservative therapy, advocated by some authors, has a higher mortality rate (Table 44). Rupture into the pleural cavity lung or bronchi which does not respond promptly to anti-amoebic therapy should also be treated surgically with appropriate intercostal tube drainage and decortication. The presence of any such complication increases the mortality rate (Table 45).

Table 44

RESULTS OF TREATMENT IN AMOEBIC PERITONITIS

Therapy	Mortality Rate	
	Before 1976*	After 1976†
Conservative		14/17 (82%)
Surgical (operative)		16/52 (31%)
Total	39/80 (49%)	30/69 (43%)

*From Wallace et al. (1978)

†Collected series (1977-1980)

Table 45

Amebic Liver Abscess and its Complications (1955-1974)

	Cases	Deaths
Uncomplicated liver abscess	1859	13 (0.7%)
Complicated by extension into		
The chest	146	9 (6.2%)
Peritonitis	38	7 (18.4%)
Complicated by extension into		
Pericardium	27	8 (29.6%)
Rupture into bowel	2 (+1*)	1 (+1*)
Hemobilia	1	0
Brain abscess	1	1
	2074	39 (1.9%)

* Rupture into pericardium and stomach.

From Adams and MacLeod (1977)

PROGNOSIS: Amoebic Abscess

Total resolution time of amoebic abscesses, with or without evacuation of abscess contents, varies from one to twelve months. The resolution time, as estimated by radionuclide scanning, correlates poorly with the initial size of the abscess cavity and is unaltered by the type of therapy. The persistence of a defect on scan for long intervals does not necessarily indicate failure of therapy since it may be associated with no clinical or chemical evidence of disease. When diagnosed, uncomplicated amoebic abscess responds to effective therapy and the mortality rate is low (Table 45). The presence of one or more of a number of findings at presentation is statistically associated with poor prognosis. These include jaundice, hepatic failure and coincident acute amoebic dysentery. In 4 reports, totalling 74 patients with jaundice, the mortality rate was 49%. In addition, extension outside the liver and the presence of multiple or left lobe abscesses are associated with increased mortality.

ANTIBIOTIC THERAPY: Pyogenic Abscess

Pyogenic liver abscesses are treated with appropriate antibiotics and, in most cases, drainage of the abscess. Choice of antibiotic regimens should be based on a clinical awareness of the spectrum of organisms common to pyogenic liver abscesses. Broad-spectrum coverage is indicated since enteric gram-negative bacteria and gram-positive cocci are commonly encountered. Infections of known biliary or portal origin contribute most of the cases of gram negative infection. An appropriate aminoglycoside antibiotic such as gentamicin or tobramycin should be used for pyogenic abscess from a gastrointestinal source. Cryptogenic abscesses and secondary infection of malignant deposits in the liver are frequently due to anaerobes. The addition of clindamycin will provide antibiotic coverage for many anaerobic species. Alternatively chloramphenicol or cefoxitin, both of which achieve high concentrations in the biliary system, can provide broad-spectrum therapy for both aerobic and anaerobic enteric organisms. Staphylococci and streptococci are encountered in hematogenous pyogenic abscess and the use of high

concentrations of penicillin together with an aminoglycoside can give good responses. Blood cultures may not be positive, even with appropriate cultures for both aerobic and anaerobic infection. Cultures of pus obtained from the abscess, even after commencement of antibiotic therapy, can be extremely helpful in directing the choice of antibiotic. Antibiotic therapy should be continued for 4-6 weeks.

SURGICAL THERAPY: Pyogenic Abscess

Undiagnosed, the mortality rate for pyogenic abscesses is 100% (Table 46). Undrained, the figures were similar until recently. Appropriate treatment of a primary intra-abdominal source of infection such as by drainage of the biliary tract or resection of bowel etc. is accepted by all. Drainage of the coexistant hepatic abscess can be established at the same time. Controversy exists regarding both the necessity of, and the best method to obtain, drainage of pyogenic liver abscesses. In 1979, Maher et al. published their experience in successfully treating 5 patients with pyogenic hepatic abscess with antibiotics alone. A sixth patient was treated with antibiotics and repeated percutaneous aspiration. The only other comparable data is from Price and colleagues at UCLA who had 6 survivors in 20 patients treated conservatively for liver abscess.

Table 46

PROGNOSIS IN HEPATIC ABSCESS*

Therapy	# Patients	(Mortality)
Nil (undiagnosed)	18/18	100%
Antibiotics	40/41	98%
Antibiotics + drainage: all	34/99	34%
solitary abscess	5/55	9%
multiple abscesses	29/44	66%
Total	92/158	58%

*Collected series (1975-1980)

The use of percutaneous aspiration or drainage has been discussed since 1953 when McFadzean et al. from Hong Kong reported on successful treatment of solitary pyogenic abscess with antibiotics and repeated aspiration. A later follow-up of their patients revealed successful treatment without surgical drainage in 107 of 108 patients. Their patient population differs from most recent series in that all patients were under 50 years of age. This may in part explain the low mortality rate. The results also emphasize the clinical observation that solitary abscesses have a better prognosis. Even before the advent of antibiotics, solitary abscesses could be adequately treated (Table 47).

Table 47

RESPONSE TO TREATMENT IN PYOGENIC ABSCESS

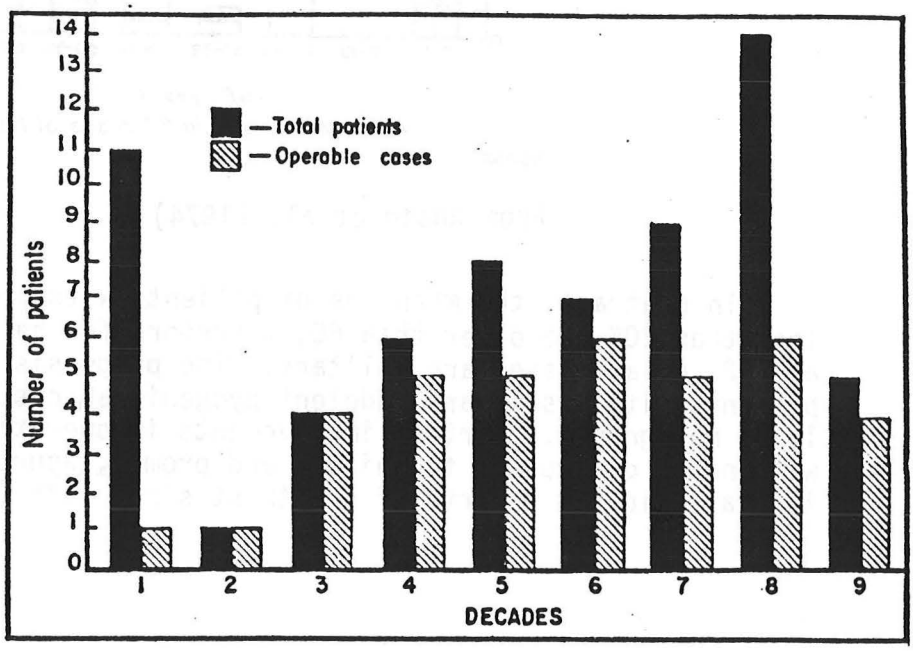
Author	Type	Treatment	Mortality Rate
Perutz*: 1893	solitary	drainage	44/182 (24%)
Elsberg: 1906	solitary	drainage	5/18 (28%)
Rothenberg and Linder: 1934	solitary	drainage	10/24 (42%)
Ochsner et al.: 1938	solitary	drainage	9/24 (38%)
	multiple	drainage	19/20 (95%)
FcFadzean et al.: 1953	solitary	antibiotics + aspir.	0/14 (0%)
			1/108 (0.9%)†
McDonald and Howard*: 1980	solitary	antibiotics + drain.	28/117 (24%)
	multiple	antibiotics + drain.	106/140 (76%)

*Collected series

†Follow-up to 1964

Percutaneous drainage as an alternative to repeated aspiration has been suggested for non-operative therapy. Martin et al. (1981) have used this method in 5 patients with pyogenic abscess. Two patients, one with an infected cyst, the other an infected hematoma, required additional surgical drainage. There was no mortality and patients were hospitalized for shorter periods of time than normally reported. This method of treatment, if the expertise is available, may be suitable for selected patients. As mentioned above, it does not replace definitive surgery for intra-abdominal conditions. There have been similar, isolated reports of successful treatment of multiple abscesses of biliary tract origin by percutaneous drainage. In the cases reported by Takeda et al. (1974), Nakayama et al. (1978) and Ferucci et al. (1980), there was drainage of multiple abscesses with resolution.

Figure XIV



Comparing by decades the incidence of patients in total series with that of group 1 or operable cases. Group 2 cases are represented by distance between top of hatched bars (operable cases) and top of solid bars (total patients).

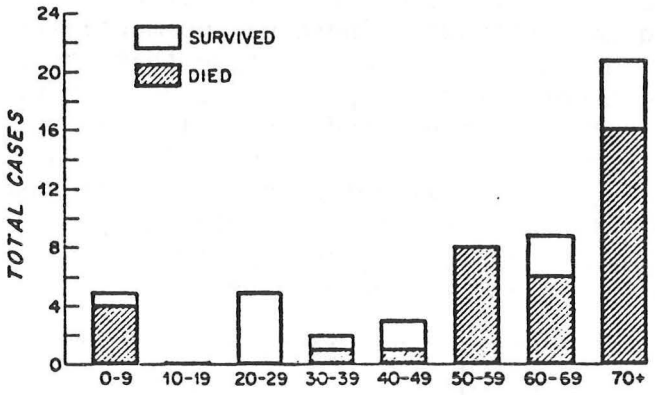
Solitary pyogenic abscesses are more amenable to surgical drainage than are multiple large abscesses but success has been reported with both (Table 46). The small macroscopic and microscopic abscesses seen with septicemia and some other etiologic agents cannot be successfully drained. These latter abscesses, in addition to poorer general health, increase the proportion of very young and very old patients regarded as non-surgical (Figure XIV). The operative approach to pyogenic liver abscesses should be directed by preoperative localization of the lesion. Some abscesses in the right lobe are best approached with rib resection and posterior drainage. Most other abscesses are best drained by a transabdominal route. This method was dangerous before antibiotic therapy was available but now the advantages of better exposure and visualization (thus permitting more adequate drainage) make it preferable to an extraserosal approach.

PROGNOSIS: Pyogenic Abscess

The mortality rate remains high in pyogenic abscess. There are a number of factors contributing to this:

a) Age of patients - mean age 51.6 years; 45% >60 years (Fig XV)
b) Presence of associated diseases - malignancy, diabetes
c) Multiple abscesses - occur in 50%, many not amenable to drainage

Figure XV



Age and mortality in 53 cases of hepatic abscess.

From Rubin et al. (1974)

In contrast, the mean age of patients with amoebic abscess is 33 years; less than 20% are older than 60, therefore few have associated diseases and 92% of abscesses are solitary. The prognosis may be excellent for patients with a solitary indolent pyogenic abscess uncomplicated by underlying malignancy. Further improvements in operative therapy can be made with newer diagnostic techniques and prompt, appropriate therapy, as illustrated in the reports of treatment since 1975 (Table 46).

SUMMARY

Hepatic abscesses have been recognized since ancient times. They continue to be associated with substantial morbidity and mortality, being invariably fatal if undiagnosed and untreated. New diagnostic and therapeutic techniques have improved the outlook, however, unless the diagnosis is considered and they are utilized, the prognosis remains poor.

ACKNOWLEDGMENTS

I would like to thank Dr. M. Landay, Dr. W. Turner and the various departments in Parkland Memorial Hospital for assistance in reviewing local experience, Marty Burgin and the Medical Illustration Services for art and photography and Mrs. Renate Davis for preparing the protocol.

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