

# Pancreatic abscess with a profound leukemoid reaction: Report of case

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**Pancreatic abscess has an attendant mortality of 60 to 70 percent with treatment and 90 to 100 percent without treatment. Early diagnosis is difficult and must be searched for in all patients whose symptoms do not resolve within 7 days of onset. In the case reported there was an unusual clinical presentation and a profound leukemoid reaction.**

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Pancreatic abscess is a lethal complication of pancreatitis.<sup>1-5</sup> Its early diagnosis is difficult and must be suspected and searched for diligently. Because of this, treatment is often less than rewarding. There is a mortality of 60 to 70 percent with therapy<sup>6</sup> and 90 to 100 percent without therapy.<sup>6</sup> Therefore, a high index of suspicion is mandatory, particularly in patients whose symptoms do not resolve within 7 days of onset.

A case is presented of pancreatic abscess with a bizarre clinical presentation and with an interesting feature of leukemoid reaction, the degree of which has not been previously reported with pancreatic abscess.

## Report of case

A 72-year-old white woman was admitted to John F. Kennedy Memorial Hospital with crampy lower left quadrant pain of 8 hours' duration associated with nausea and vomiting. The patient had been in her usual state of health prior to the onset of these symptoms. The pain was described as crampy and most severe in the left lower quadrant with minimal radiation to the epigastrium. The pain was not affected by position and was not relieved or improved with vomiting. There was no complaint of vomiting of blood.

Past medical history was positive for a previous attack of diverticulitis 7 years prior to this admission. The past surgical history was negative. The patient was taking no medications.

Physical examination on admission revealed an obese woman in moderate distress. The head, eyes, ears, nose, and throat were unremarkable. There was no evidence of jaundice. The lungs were clear. The heart rate was rapid and the rhythm was regular without any sig-

nificant murmurs. The abdominal examination showed left lower quadrant tenderness with voluntary guarding. No masses were palpable and there were no local peritoneal signs. The extremities were unremarkable. A rectal examination was negative. Stool was negative for occult blood. Pelvic examination was unremarkable. The initial laboratory results showed a leukocyte count of 16,000/cu. mm. with a shift to the left. The serum amylase level was 82, with a normal urinary amylase creatinine ratio.

The patient was admitted with a provisional diagnosis of diverticulitis and was treated conservatively with fluid and antibiotics and seemed to be doing well. Late on the second hospital day, she suddenly developed shortness of breath, diaphoresis, and hypotension. She was placed in the medical intensive care unit and was noted to have a supraventricular tachycardia. Blood gases at that time showed pH of 7.30, PO<sub>2</sub> of 52, and PCO<sub>2</sub> of 26. She was treated with oxygen, fluids, and propranolol, and 6 hours later was improving. Abdominal findings at the time of the acute devolution were benign, but a serum amylase drawn at that time was 632. Over the next few hours the patient continued to have diffuse abdominal pain without any peritoneal signs. Mesenteric infarction was considered. A peritoneal lavage was performed and there was no evidence of any blood, pus, or organisms. An amylase determination of the peritoneal fluid was 76. The leukocytosis progressively rose from 16,000/cu. mm. on admission to 42,000 early on the second hospital day to 77,000 at the time of the acute episode and subsequently rose to 92,000 on the sixth hospital day. Fifteen percent myelocytes and 10 percent metamyelocytes were noted in the peripheral smear. Because of the presence of fever, hyperamylasemia, subsequent hypocalcemia, and septicemia, a diagnosis of pancreatic abscess was entertained. Hematology consultation for the elevated leukocyte count was obtained, and a bone marrow biopsy was felt to be compatible with a leukemoid reaction and not due to acute leukemia. A leukocyte alkaline phosphatase at that time was 189. Early blood cultures were negative and a later culture from the fourth hospital day was positive for *Staphylococcus aureus*. Serum amylase fell to normal within 48 hours of the acute episode.

The patient continued to devolute despite aggressive medical support with fluids, antibiotics, total parenteral nutrition, cimetidine, mechanical ventilation, and Swan-Ganz catheterization. Real time ultrasound of the gallbladder, biliary tree, and pancreas was unremarkable. The surgery department was consulted for drainage of the suspected pancreatic abscess, but this was declined because of the debilitated condition of the patient. The patient continued to devolute with fever, pulmo-



nary insufficiency, and renal failure. She was transferred to another institution for hemodialysis. After slight improvement, surgery was performed. At laparotomy there was confirmation of the clinical suspicion of pancreatic abscess. There was no evidence of peridiverticular abscess. The patient did poorly postoperatively, becoming more obtunded, and she was found to have *Candida* growing in her cerebrospinal fluid. She subsequently died 27 days after the onset of acute symptoms.

## Discussion

### *Pathophysiology*

Pancreatic abscesses are collections of necrotic debris and pus within the pancreas or extending from it.<sup>6</sup> If areas of necrosis develop during acute pancreatitis, a foci for possible abscess is set up. The exact mechanism by which bacteria gain access is not completely known. Several theories include hematogenous spread, lymphatic spread from the gallbladder or colon, and direct transmural penetration from the transverse colon.<sup>6</sup> Usually the abscess is confined to the retroperitoneum, but at times it may occur in the lesser omental sac and result in subphrenic abscess as well. Also, a retroperitoneal abscess may extend along the retroperitoneal fascial planes and extend into the mediastinum or into the transverse colon, small bowel mesentery, or scrotum.<sup>3</sup>

### *Clinical manifestations*

Pancreatic abscess is a complication of acute pancreatitis in about 4 percent of the cases.<sup>1</sup> A high index of suspicion is needed to make a diagnosis of pancreatic abscess early. Any patient with acute pancreatitis who has persistent fever, abdominal tenderness, or an abdominal mass and clinical deterioration 1 to 4 weeks after the acute attack should be strongly considered for development of pancreatic abscess. A second clinical presentation is that of a patient with acute pancreatitis with clinical deterioration in the first 72 to 96 hours.<sup>6</sup> The usual clinical manifestations are fever, 38-40 C, a mass in approximately 50 percent of the cases, leukocytosis usually between 15,000 and 20,000/cu. mm., and abdominal pain which is usually epigastric and radiating to the back. More variable findings are hyperbilirubinemia and an elevated alkaline phosphatase.<sup>3</sup> Serum amylase is not consistently elevated and may be normal.

### *Bacteriology of pancreatic abscess*

The most common organisms found in pancreatic abscesses are the enteric organisms. These include *Escherichia coli*, *Klebsiella*, and *enterococcus*. Other organisms that have been isolated include *Proteus*, *Staphylococcus*, and *Pseudomonas*.<sup>1-6</sup> It is interesting to note that in 50 percent of the cases cultures are polymicrobial. Anaerobic abscesses have been isolated in only a few instances. This

may be related to the fact that anaerobic techniques may be too insensitive and that in the future with better techniques, more anaerobic infections will be isolated. Also, antibiotics used in treatment of these patients may prevent identification.<sup>7</sup>

### *Radiology of pancreatic abscesses*

Flat plate of the abdomen may be helpful in cases of suspected pancreatic abscess. Felson<sup>8</sup> described a "soap-bubble" appearance in the area of the pancreas. These "bubbles" represent retroperitoneal abscess. The upper gastrointestinal tract may demonstrate involvement of various structures. The stomach may be displaced anteriorly, the duodenal loop may be widened, or there may be obstruction of the duodenum. There may be also downward displacement of the ligament of Treitz. The barium enema examinations might show the transverse colon and splenic flexure downwardly displaced. An intravenous pyelogram may show the left kidney depressed. A CAT scan of the abdomen and ultrasound of the abdomen are very helpful, noninvasive techniques.<sup>15</sup> They will show areas of pancreatic enlargement and multiple ill-defined areas inside the abscess cavity. The abscess cavity is usually irregular in shape with a thickened rim; therefore, it is possible to differentiate abscess from pancreatic pseudocyst.<sup>8,9,10</sup> At times, selective abdominal angiography may be helpful in localizing an abscess.<sup>11</sup> A chest x-ray might show an elevated diaphragm, pleural effusion, or atelectasis of the lower lobes of the lung.

## Complications

Often other abscesses elsewhere in the pancreas or retroperitoneum go undiagnosed at laparotomy. There may be free perforation of a pancreatic abscess into the peritoneal cavity and this is usually fatal.<sup>1,3</sup> There may be perforation into other intra-abdominal organs such as the stomach, duodenum, colon, or biliary tree.<sup>2</sup> These perforations are usually associated with massive gastrointestinal bleeding. Gastrointestinal bleeding may also be secondary to erosive lesions in the stomach and duodenum. There may also be erosion of a major artery which can cause bleeding into the pancreatic abscess.<sup>1,3</sup> Pulmonary complications include empyema secondary to an infected pleural effusion<sup>5</sup> and hemoptysis secondary to perforation of an abscess into a bronchus.<sup>3</sup> Rarely one may see bacterial endocarditis.<sup>6</sup> Glucose intolerance may be transient or permanent depending on the extent of pancreatic endocrine destruction.<sup>1,4</sup>

### *Treatment of pancreatic abscess*

Prevention of pancreatic abscess must be emphasized.<sup>12</sup> A high index of suspicion in all cases of



pancreatitis which do not resolve as expected would lead to earlier diagnosis and thus prevent morbidity and mortality. Once formed, drainage of all abscesses is paramount. Survival without surgical drainage is less than 5 percent.<sup>1,13</sup> An overall survival rate with drainage is 65-70 percent.<sup>14</sup> A second operation may be necessary to remove further necrotic debris or to drain recurrent abscesses.<sup>7,15</sup> Antibiotic therapy is indicated but should not be the sole form of therapy. Penicillin and chloromycetin seem to be the drugs of choice. The drains should be left in for one week and then gradually removed.<sup>6</sup> During this period of recovery, total parenteral nutrition is necessary to maintain the patient in positive nitrogen balance; however, glucose intolerance must be watched for with this modality.

Our case is most interesting because of the presentation of left lower quadrant pain which was initially felt to represent diverticulitis with subsequent septicemia and pancreatic abscess. It is possible that the abscess was secondary to a ruptured diverticulum but since no microperforation of the colon was noted at laparotomy and there was no pericolic abscess, this etiology seemed untenable. More likely, the patient had acute idiopathic pancreatitis which was complicated by pancreatic abscess. It is well known that with inflammation of the tail of the pancreas, pain can radiate into the left lower quadrant. We believe that this explains our patient's left lower quadrant discomfort. What is more interesting is the extreme leukemoid reaction. In all the literature reviewed, no previously recorded case of pancreatic abscess has shown the degree of leukocytosis that was seen in our patient.

Leukemoid reaction was first described by Krumbhaar in 1926.<sup>16</sup> It is a general term that is used to describe a peripheral blood picture that resembles leukemia but in which the bone marrow is not suggestive of leukemia. At times, the differentiation may be difficult and the only way true leukemia can be ruled out is by observation of the patient for a period of time or with return of the peripheral leukocytosis to normal.

Leukemoid reactions are usually phenomenon secondary to infection but may be seen with malignancy. Any cell line may be affected.<sup>17</sup>

Granulocytic leukemoid reactions characteristically have high leukocyte alkaline phosphatase levels, while those with chronic myelocytic leukemia have low scores.<sup>18</sup> In our patient, the leukocyte alkaline phosphatase level was elevated and the bone marrow did not show the hypercellularity associated with leukemia.

Etiology of leukemoid reactions is not clearly understood. One theory is that toxins are released either by the tumor or the infectious process. Another theory is dyshematopoiesis associated with

bone marrow metastasis.<sup>17</sup> Sometimes falsely positive leukocytosis is produced by the use of automated blood counters. Cryoprotein may aggregate when the blood is cooled and result in false leukocytosis due to counting of the protein crystals.<sup>19,20</sup>

It is important to stress that once the diagnosis of pancreatic abscess is made, immediate surgical drainage is needed. We agree with Donahue and associates<sup>14</sup> who stated that the typical situation in a patient with pancreatic abscess is that the patient is considered too sick to have surgical exploration when in fact the patient is too ill *not* to be operated on. Without surgical drainage, the patient's chance for survival is almost nil.

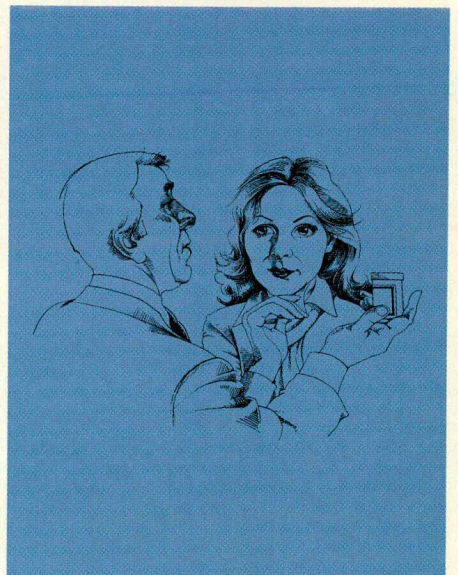
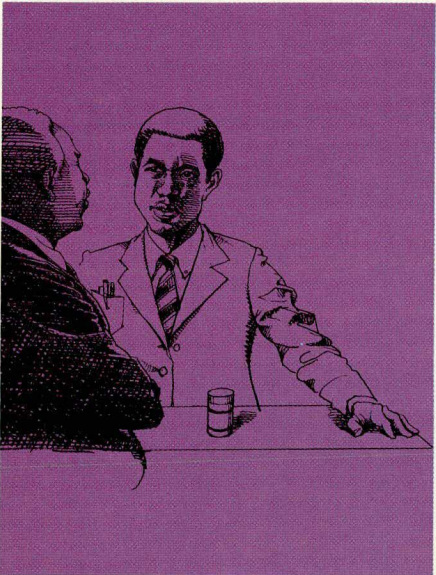
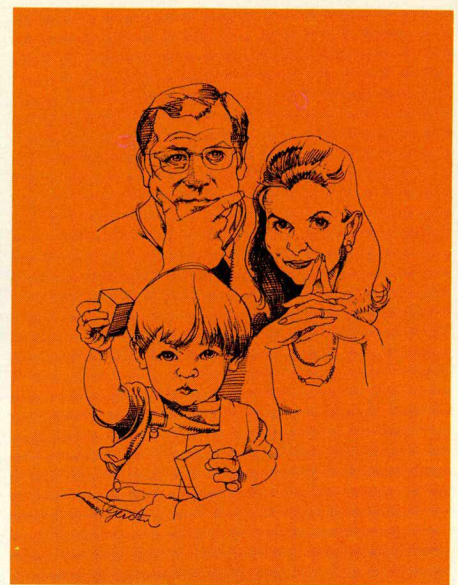
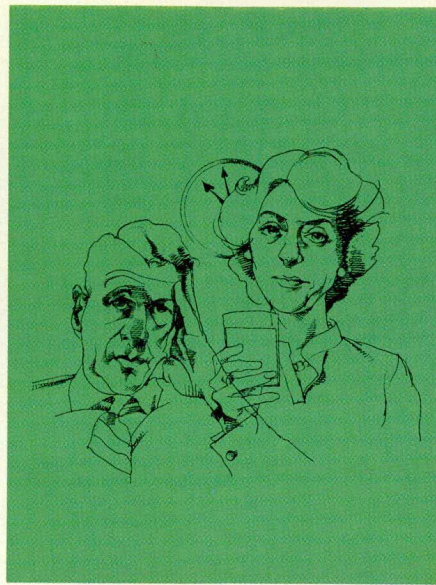
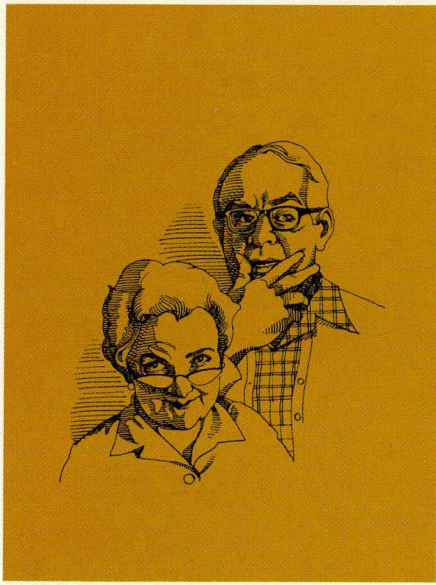
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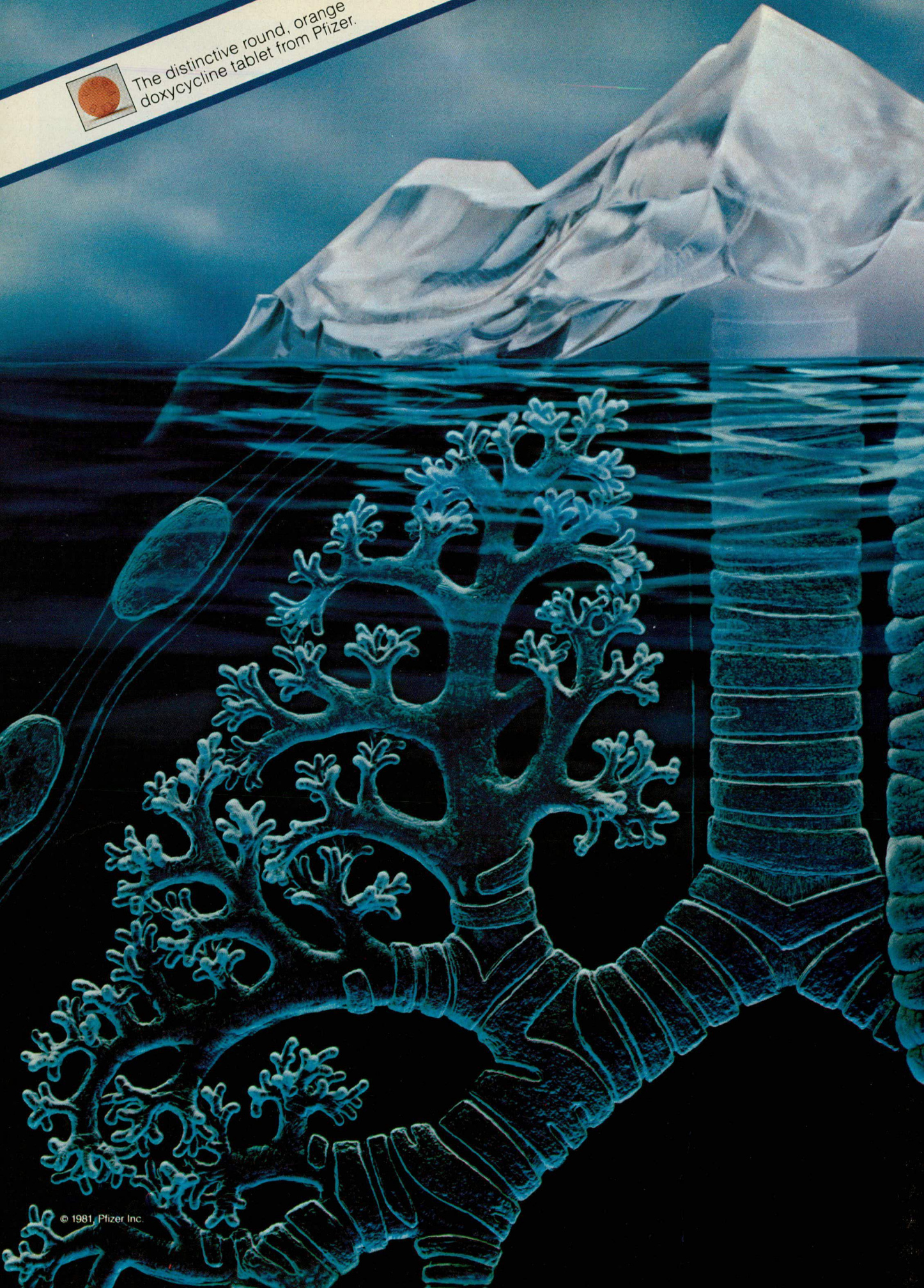
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<sup>1</sup> Fulco OJ: The respiratory system as a unit: An overview of sinobronchial infections. Respiratory infections: Update on the role of Vibramycin<sup>®</sup> (doxycycline) in the treatment of sinobronchial infections and pneumonias. *Postgrad Med (suppl)*, January 1981, pp 20-29.

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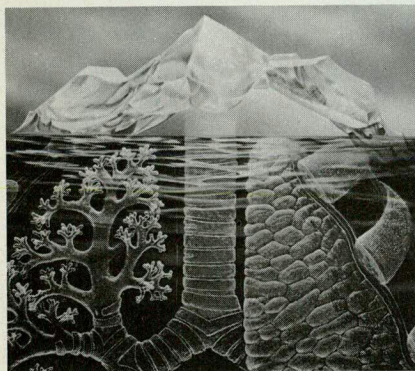




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**Warnings:** THE USE OF DRUGS OF THE TETRACYCLINE CLASS DURING TOOTH DEVELOPMENT (LAST HALF OF PREGNANCY, INFANCY AND CHILDHOOD TO THE AGE OF 8 YEARS) MAY CAUSE PERMANENT DISCOLORATION OF THE TEETH (YELLOW-GRAY-BROWN). This adverse reaction is more common during long-term use of the drugs, but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported. **TETRACYCLINE DRUGS, THEREFORE, SHOULD NOT BE USED IN THIS AGE GROUP UNLESS OTHER DRUGS ARE NOT LIKELY TO BE EFFECTIVE OR ARE CONTRAINDICATED.**

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be advised that this reaction can occur with tetracycline drugs, and treatment should be discontinued at the first evidence of skin erythema.

The antianabolic action of the tetracyclines may cause an increase in BUN. Studies to date indicate that this does not occur with the use of doxycycline in patients with impaired renal function.

**Usage in Pregnancy:** (See above "Warnings" about use during tooth development.) Animal studies indicate that tetracyclines cross the placenta, are found in fetal tissues and can have toxic effects on the developing fetus (often related to retardation of skeletal development). Evidence of embryotoxicity has also been noted in animals treated early in pregnancy.

**Usage in Newborns, Infants and Children:** (See above "Warnings" about use during tooth development.)

As with other tetracyclines, doxycycline forms a stable calcium complex in any bone-forming tissue. A decrease in fibular growth rate has been observed in premature given oral tetracycline, 25 mg/kg q6h, but this reaction was shown to be

reversible when the drug was discontinued.

Tetracyclines are present in the milk of lactating women who are taking a drug in this class.

**Precautions:** As with other antibiotics, overgrowth of nonsusceptible organisms may occur, including fungi. If superinfection occurs, discontinue the antibiotic and institute appropriate therapy.

In venereal disease when coexistent syphilis is suspected, a dark-field examination should be done before initiating therapy. Conduct monthly serological tests for at least 4 months.

Because tetracyclines depress plasma prothrombin activity, patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

In long-term therapy, periodic laboratory evaluation of organ systems, including hematopoietic, renal and hepatic studies should be performed.

Treat all group A beta-hemolytic streptococcal infections for at least 10 days. (For upper respiratory infections due to group A beta-hemolytic streptococci, penicillin is the usual drug of choice, including prophylaxis of rheumatic fever.)

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving tetracycline in conjunction with penicillin.

**Adverse Reactions:** Due to oral doxycycline's virtually complete absorption, side effects of the lower bowel, particularly diarrhea, have been infrequent. The following adverse reactions have been observed in patients receiving tetracyclines: anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region. Rare instances of esophagitis and esophageal ulcerations have been reported in patients receiving capsule and tablet forms of drugs in the tetracycline class. Most of these patients took medications immediately before going to bed. (See "Dosage and Administration.") Maculopapular and erythematous rashes, exfoliative dermatitis, photosensitivity (see "Warnings"), urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus, hemolytic anemia, thrombocytopenia, neutropenia and eosinophilia have been reported. Prolonged administration of tetracyclines may produce brown-black microscopic discoloration of thyroid glands. No abnormalities of thyroid function studies are known to occur.

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■ Can be used without dosage alteration in patients with impaired renal function.

Rise in BUN has been reported and is apparently dose related. (See "Warnings.")

**Dosage and Administration:** DOSAGE AND FREQUENCY OF ADMINISTRATION OF DOXYCYCLINE DIFFERS FROM THAT OF OTHER TETRACYCLINES. EXCEEDING THE RECOMMENDED DOSAGE MAY RESULT IN AN INCREASED INCIDENCE OF SIDE EFFECTS.

Adults: The usual dose of Vibramycin is 200 mg on the first day of treatment (administered 100 mg every 12 hours) followed by a maintenance dose of 100 mg/day. The maintenance dose may be administered as a single dose or as 50 mg every 12 hours. In more severe infections (particularly chronic infections of the urinary tract), 100 mg every 12 hours is recommended.

For children above eight years of age: See package insert for recommended dosage schedules.

Acute gonococcal infections (when penicillin is contraindicated): 200 mg stat, and 100 mg at bedtime, the first day, followed by 100 mg *b.i.d.* for 3 days.

As an alternate single-visit dose, administer 300 mg stat followed in one hour by a second 300-mg dose. The dose may be administered with food, including milk or carbonated beverage, as required.

Primary and secondary syphilis (when penicillin is contraindicated): 300 mg a day in divided doses for at least 10 days.

When used in streptococcal infections, therapy should be continued for 10 days.

Administration of adequate amounts of fluid along with capsule and tablet forms of drugs in the tetracycline class is recommended to wash down the drugs and reduce the risk of esophageal irritation and ulceration. (See "Adverse Reactions.") It is recommended that Vibramycin be given with food or milk to reduce the possibility of gastric irritation. The absorption of Vibramycin is not markedly influenced by simultaneous ingestion of food or milk.

Concomitant therapy: Antacids containing aluminum, calcium, or magnesium impair absorption and should not be given to patients taking oral Vibramycin.

Studies to date have indicated that administration of Vibramycin at the usual recommended doses does not lead to excessive accumulation of the antibiotic in patients with renal impairment.

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