
Family Practice Grand Rounds

Postpartum Pulmonary Embolism

Gary Enders, MD, Larry Novak, MD, Mary Studdiford, ACSW, and James B. Tucker, MD
Syracuse, New York

DR. LARRY NOVAK (*Associate Professor, Department of Family Practice*): Today we want to discuss a common medical problem, pulmonary embolism, in an uncommon host, a healthy postpartum family practice patient, and how hospitalization affects the maternal-child relationship. Dr. Enders and I have followed this family in the family practice center and hospital. He will present the case.

DR. GARY ENDERS (*Third-year Family Practice Resident*): Nancy C. is a healthy 21-year-old, gravida 2, para 2, woman who had a normal, spontaneous vaginal delivery at term. She had a

normal prenatal course and had no risk factors for thromboembolic disease. She is slender, gained only 29 lb with the pregnancy, had no varicosities, is a nonsmoker, and had an uncomplicated 16-hour labor. Nine hours later she complained of shortness of breath and chest pain while walking to the bathroom. On examination, her respiratory rate was 36/min, pulse 130 beats/min, and systolic blood pressure was palpable at 70 mmHg. There was no excess uterine bleeding or tenderness of her legs. Her hematocrit was unchanged at 38 percent. Arterial blood gases showed a pH of 7.43, PCO₂ of 30 mmHg, and PO₂ of only 46 mmHg. An electrocardiogram showed sinus tachycardia, and incomplete right bundle branch block, with a S₁Q₃ complex. Her chest roentgenogram revealed scoliosis with clear lung fields. A lung scan done immediately thereafter showed three perfusion defects in the left lung and one perfusion defect in

Continued on page 351

From the Family Practice Residency, St. Joseph's Hospital Health Center, and the Department of Family Practice, Upstate Medical Center, State University of New York, Syracuse, New York. Requests for reprints should be addressed to Dr. Larry Novak, Department of Family Practice, SUNY Upstate Medical Center, 301 Prospect Avenue, Syracuse, NY 13203.

Azo Gantrisin®
Each tablet contains 0.5 Gm sulfisoxazole/Roche and 50 mg phenazopyridine HCl.

Before prescribing, please consult complete product information, a summary of which follows:

INDICATIONS: Initial treatment of uncomplicated urinary tract infections caused by susceptible strains of *Escherichia coli*, *Klebsiella* species, *Enterobacter* species, *Proteus mirabilis*, *Proteus vulgaris* and *Staphylococcus aureus* when relief of pain, burning or urgency is needed during first 2 days of therapy. Azo Gantrisin treatment not to exceed 2 days. Evidence lacking that sulfisoxazole plus phenazopyridine HCl better than sulfisoxazole alone after 2 days. Treatment beyond 2 days should only be continued with Gantrisin (sulfisoxazole/Roche). (See DOSAGE AND ADMINISTRATION.) **Important Note:** Coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response. With ongoing therapy, add aminobenzoic acid to culture media. Increasing resistance of organisms may limit sulfonamide usefulness. As identical doses produce wide variations, measure blood levels in patients receiving sulfonamides for serious infections: 12 to 15 mg/100 ml is optimal; adverse reactions are more frequent above 20 mg/100 ml.

CONTRAINDICATIONS: Children under 12; known sensitivity to either component; pregnancy at term and during nursing period; in glomerulonephritis, severe hepatitis, uremia and pyelonephritis of pregnancy with gastrointestinal disturbances.

WARNINGS: Sulfonamides are bacteriostatic; organisms causing common infections are often resistant. Sulfas won't eradicate group A streptococci or prevent sequelae like rheumatic fever and glomerulonephritis. Deaths from hypersensitivity reactions, hepatocellular necrosis, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Perform blood counts and renal function tests.

PRECAUTIONS: *General:* Use with caution in patients with impaired renal or hepatic function, severe allergy, bronchial asthma. Hemolysis may occur in glucose-6-phosphate dehydrogenase-deficient individuals.

The more soluble sulfonamides are associated with fewer renal complications. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Information for Patients: Maintain adequate fluid intake; urine will turn reddish-orange. *Laboratory Tests:* Perform urinalysis with careful microscopic examination at least once a week and regular blood counts after 2 weeks therapy; measure blood levels in patients with serious infection (see INDICATIONS). *Drug Interactions:* Sulfonamides may displace oral anticoagulants from plasma protein binding sites, increasing anticoagulant effect. Can also displace methotrexate. *Drug Laboratory Test Interactions:* May affect liver function tests in hepatitis.

Carcinogenesis, Mutagenesis, Impairment of Fertility, Carcinogenesis: Azo Gantrisin has not undergone adequate trials relating to carcinogenicity; each component, however, has been evaluated separately. Rats appear especially susceptible to goitrogenic effects of sulfonamides; long-term administration has resulted in thyroid malignancies in this species. Long-term administration of phenazopyridine HCl has induced neoplasia in rats (large intestine) and mice (liver). No association between phenazopyridine HCl and human neoplasia reported; adequate epidemiological studies have not been conducted. *Mutagenesis:* No studies available. *Impairment of Fertility:* The components of Azo Gantrisin have been evaluated in animal reproduction studies. In rats given 800 mg/kg/day sulfisoxazole, there were no effects on mating behavior, conception rate or fertility index. Fertility was not affected in a two-litter study of rats given 50 mg/kg/day phenazopyridine.

Pregnancy, Teratogenic Effects: Pregnancy Category C. The components of Azo Gantrisin have been evaluated. At 800 mg/kg/day sulfisoxazole was nonteratogenic in rats and rabbits, with no perinatal or postnatal effects in rats. In two other studies, cleft palates developed in rats and mice after 500 to 1000 mg/kg/day sulfisoxazole. No congenital malformations developed in rats given 50 mg/kg/day phenazopyridine. As there are no satisfactory animal or human studies, it is not known whether Azo Gantrisin can cause fetal harm or affect reproduction capacity. Use during pregnancy only if the potential benefit justifies the potential risk to the fetus. *Nonteratogenic Effects, Nursing Mothers and Pediatric Use:* See CONTRAINDICATIONS.

ADVERSE REACTIONS: *Allergic:* Anaphylaxis, generalized allergic reactions, angioneurotic edema, arteritis and vasculitis, myocarditis, serum sickness, conjunctival and scleral injection, periarteritis nodosa, systemic lupus erythematosus. *Cardiovascular:* Tachycardia, palpitations, syncope, cyanosis. *Dermatologic:* Rash, urticaria, pruritus, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, photosensitivity. *Endocrine:* Goiter production, diuresis, hypoglycemia. Cross-sensitivity with some goitrogenic diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents may exist. *Gastrointestinal:* Nausea, emesis, abdominal pain, anorexia, diarrhea, glossitis, stomatitis, flatulence, salivary gland enlargement, G.I. hemorrhage, pseudomembranous enterocolitis, melena, pancreatitis, hepatic dysfunction, jaundice, hepatocellular necrosis. *Genitourinary:* Crystalluria, hematuria, BUN and creatinine elevation, nephritis and toxic nephrosis with oliguria and anuria, acute renal failure, urinary retention. *Hematologic:* Leukopenia, agranulocytosis, aplastic anemia, thrombocytopenia, purpura, hemolytic anemia, anemia, eosinophilia, clotting disorders including hypoprothrombinemia and hypofibrinogenemia, sulfhemoglobinemia, methemoglobinemia. *Musculoskeletal:* Arthralgia, chest pain, myalgia. *Neurologic:* Headache, dizziness, peripheral neuritis, paresthesia, convulsions, tinnitus, vertigo, ataxia, intracranial hypertension. *Psychiatric:* Psychosis, hallucinations, disorientation, depression, anxiety. *Miscellaneous:* Edema (including periorbital), pyrexia, drowsiness, weakness, fatigue, lassitude, rigors, flushing, hearing loss, insomnia, pneumonitis.

OVERDOSAGE: *Signs:* Anorexia, colic, nausea, vomiting, dizziness, drowsiness, unconsciousness; possibly pyrexia, hematuria, crystalluria. Blood dyscrasias and jaundice may occur later. *Treatment:* Institute gastric lavage or emesis; force oral fluids; administer intravenous fluids if urine output is low with normal renal function. Monitor blood counts and appropriate blood chemistries, including electrolytes. In cyanosis, consider methemoglobinemia and treat with intravenous 1% methylene blue. Institute specific therapy for blood dyscrasias or jaundice.

DOSAGE AND ADMINISTRATION: Azo Gantrisin is intended for the acute, painful phase of urinary tract infections. The recommended dosage in adults is 4 to 6 tablets initially, followed by 2 tablets four times daily for up to 2 days. Treatment with Azo Gantrisin should not exceed 2 days. Treatment beyond 2 days should only be continued with Gantrisin (sulfisoxazole/Roche).

HOW SUPPLIED: Tablets, each containing 0.5 Gm sulfisoxazole/Roche and 50 mg phenazopyridine HCl—bottles of 100 and 500.

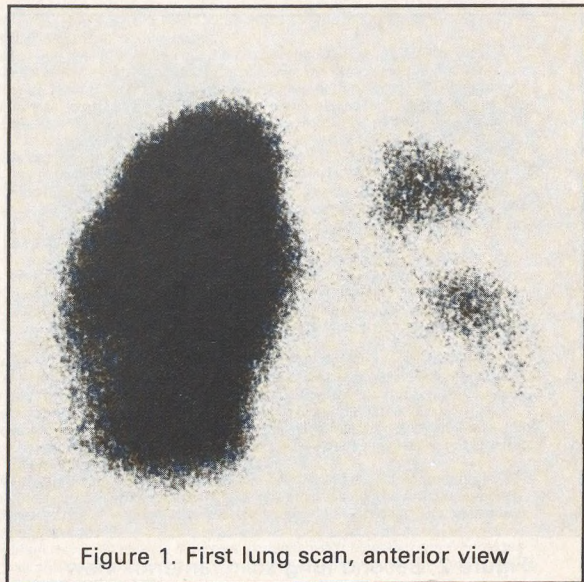


Figure 1. First lung scan, anterior view

Continued from page 349

the right lung (Figure 1). A diagnosis of acute pulmonary embolism was made, and the patient was treated with an intravenous heparin drip. The patient was strongly motivated to breast feed, so she pumped her breasts for three days until the radiopharmaceutical used for the lung scan had decayed sufficiently.¹ Then she began breast feeding.

Three days later increased uterine bleeding was noted. The hematocrit dropped to 30 percent. She was treated with methylergonovine, and the bleeding decreased. Four days later an episiotomy hematoma formed that continued to bleed despite being drained, and she required two units of blood. Her heparin drip was discontinued until the bleeding stopped and then restarted at a lower dose.

On the eighth hospital day, she was begun on high-dose subcutaneous heparin, which was continued for six weeks. The doses were given each day at 8 AM and 8 PM, and adjusted to maintain the midpoint (2 PM) partial thromboplastin time (PTT) at 1.5 to 2.0 times control. She required 11,000 units of heparin per dose to accomplish this level of control.

Mrs. C. and her baby were discharged on the

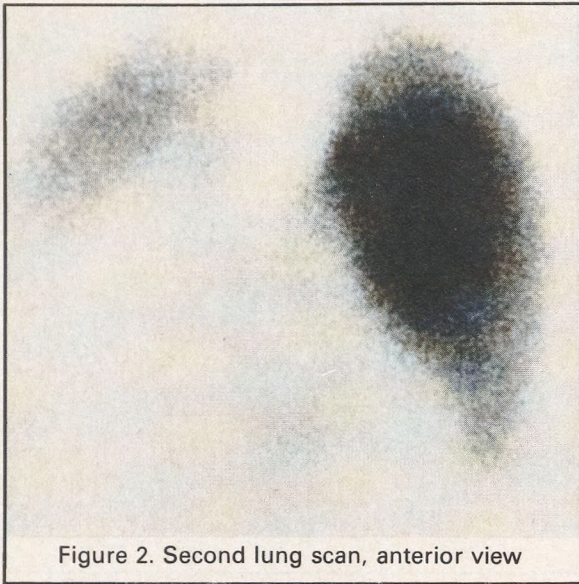


Figure 2. Second lung scan, anterior view

13th postpartum day. Mrs. C faithfully injected herself with heparin every 12 hours for the six weeks and did very well without dyspnea or other symptoms. At nine weeks of life, the baby was admitted to the hospital for two days with viral pneumonia. During the hospitalization Mrs. C. stayed overnight in a chair in her child's room. After discharge, Mrs. C. was carrying the child home when she suddenly developed shortness of breath and almost passed out. She was walking alone and barely managed to get home. She did not tell anyone about this episode until she brought her child in for a follow-up appointment a week later. At this time, Mrs. C. had a resting tachycardia of 150 beats/min and a respiratory rate of 30/min. A repeat lung scan showed almost complete loss of perfusion to the right lung (Figure 2). Cardiology and vascular surgery consultations were obtained, and further evaluation (angiography, venography) was considered, but it was felt to offer little information that would aid subsequent management. Because this second embolus was so large, intravenous streptokinase was used in an attempt to dissolve the clot rapidly. However, her thrombin time during streptokinase infusion remained baseline, and she was refractory

to this therapy. Accordingly, streptokinase was discontinued and heparin begun. After six days, warfarin was started, and anticoagulation for at least six months was planned. An echocardiogram showed mitral valve prolapse and indicated possible pulmonary hypertension. She was discharged on the 12th hospital day. She slowly improved her exercise tolerance and proceeded to get back to normal. Because of her severe progressive scoliosis, she faces surgery in the future and probably will be in a body cast for six months.

The incidence of pulmonary embolism in the United States is estimated to be 650,000 per year.² Mortality is approximately 38 percent, and mortality is five to six times greater when the diagnosis is initially missed. Approximately 10 percent of those affected die in the first hour.

The risk of pulmonary embolism during pregnancy is only 1/100,000. In the postpartum state, hypercoagulability, loss of venous tone, and decreased physical activity place a woman at a somewhat greater risk—about 5/10,000.³ Thromboembolism may stem from thrombophlebitis of pelvic or leg veins.

Heparin is the drug of choice for the treatment of pulmonary embolism during pregnancy. Warfarin is contraindicated, since it can cross the placenta and cause hemorrhagic complications in the fetus. The safety and effectiveness of adjusted-dose subcutaneous heparin for the long-term management of deep venous thrombosis has been documented by Hull et al.⁴ In this study 106 patients with acute, proximal venous thrombosis confirmed by venogram and treated with conventional intravenous heparin were then randomized to either adjusted-dose heparin or warfarin for secondary prophylaxis. Two of the 53 patients receiving heparin, compared with 1 of the 53 receiving warfarin, had new episodes of thromboembolism. Nine patients taking warfarin had bleeding complications compared with one patient taking heparin. In the protocol described by Hull et al, heparin was given every 12 hours in adjusted doses, so the PTT taken six hours after a dose was 1.5 times control. After initial adjustments were made, there were no further changes in the heparin doses.

Since heparin does not pass into breast milk, it is safe for nursing mothers and was used in our

Continued on page 354

Continued from page 352

patient. I felt that the use of warfarin while breast feeding was more risky. A British study, however, indicates that warfarin is probably also safe for nursing mothers.⁵ In this study, warfarin could not be detected in the breast milk of 13 mothers taking it postpartum. Seven of the 13 mothers were breast feeding their infants; warfarin could not be detected in the serum of any of these infants. Three of these seven infants were measured for anticoagulant effect in their plasma; one of these infants was mildly affected at day 3 of life, but this improved slightly by day 7.

Warfarin is a weak acid (pH 5.0) and thus is present in ionized form at body pH. Warfarin is strongly bound to plasma proteins. Since warfarin is ionized, it has difficulty passing through the lipid barrier of the breast epithelium. The study concludes that warfarin is probably safe when given to breast-feeding mothers, but it would probably be advisable to monitor the prothrombin time (PT) of the infant.

DR. NOVAK: Did Mrs. C. consider switching to formula rather than breast feeding?

DR. ENDERS: She was very strongly motivated to breast feed. She did not breast feed her first child and had really anticipated breast feeding her second child.

RESIDENT IN THE AUDIENCE: Do you think it would be safer for the mother to take warfarin if the child was given a vitamin K preparation?

DR. ENDERS: Yes, that sounds like a good idea, since vitamin K counteracts the effects of warfarin.

DR. NOVAK: Are there any questions in regard to the home treatment?

THIRD-YEAR FAMILY PRACTICE RESIDENT: How did you decide to start with subcutaneous heparin in regard to dosage? Did you just pick a dose?

DR. ENDERS: One method is to total the amount of intravenous heparin given within 24 hours and then divide this into two doses. Dr. Hull and his colleagues found that the average dose of subcutaneous heparin required when given every 12 hours was 10,000 units. This is a good place to start.

FIRST-YEAR FAMILY PRACTICE RESIDENT: How did you follow up with laboratory testing?

DR. ENDERS: Six hours after the subcutane-

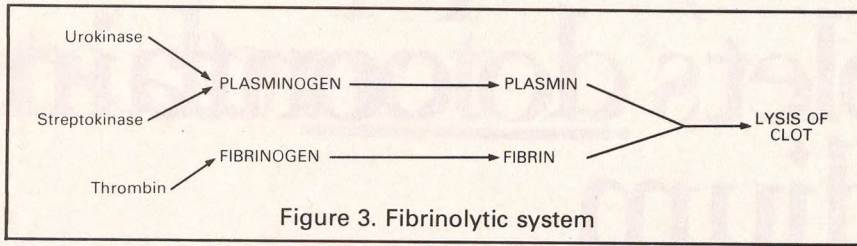
ous heparin injection, the PTT is measured and the dose is adjusted to make the PTT 1.5 times control. Once adjusted in the hospital, no further measurements are required. One benefit of twice daily heparin injections, as compared with warfarin, is that periodic anticoagulant tests are not needed, as shown in the study by Hull and colleagues.

Now I would like to discuss fibrinolytic therapy. The human hemostatic system is closely regulated and has the capacity of breaking down blood clots through the plasminogen-plasmin system (Figure 3). Plasminogen is an inactive proenzyme that can be activated to plasmin by certain endogenous stimuli. Plasmin is a very active enzyme that breaks down protein including fibrin clots. Both thrombolytic agents, urokinase and streptokinase, activate this endogenous fibrinolytic system. Urokinase is an enzyme derived from human kidney cells that cleaves two peptide bonds of plasminogen, forming plasmin.⁶ Urokinase is much more expensive and less available than streptokinase. Streptokinase is a nonenzymatic protein produced by group C beta-hemolytic streptococci. Streptokinase forms an active complex with plasminogen, and this complex converts other plasminogen molecules to plasmin.

Most authors feel that thrombolytic therapy should be reserved for massive pulmonary embolism.^{6,7} Our patient had a fairly large recurrent embolism in the setting of significant restrictive lung disease secondary to her scoliosis. She was probably not an ideal candidate for thrombolytic therapy, however, since her embolism was more than seven days old on admission to the hospital. After approximately five days, the fibrin clot becomes organized and somewhat resistant to lysis by plasmin.

DR. JAMES TUCKER (*Associate Professor, Department of Family Practice*): Did you discuss future pregnancy with the family?

DR. ENDERS: Yes. Certainly she would be considered high risk for recurrent thromboembolic disease with future pregnancy. We discussed with her and her husband the need for subcutaneous heparin anticoagulation during the latter part of any future pregnancy. After her second embolus, however, Mrs. C. decided against future pregnancy and is now planning a tubal ligation, since she has two children already.



Although we assume that the changes in pregnancy and the postpartum period predisposed Nancy C. to thromboemboli, I would still consider her at greater risk in the future for nonpregnancy-related emboli than someone who had not had these problems. We would not suggest long-term coumarin therapy, and aspirin, dipyridamole, and sulfipyrazone have not been shown to be effective in preventing recurrent pulmonary emboli. However, we would certainly not disagree with anyone who suggested long-term use of support stockings and avoiding prolonged sitting and external pressure to the legs.

DR. NOVAK: This brings up the problem of a hospitalized parent with a young child or children at home. Mary Studdiford will now discuss some things that can be done in the hospital or at home to try to keep families functioning during these difficult times.

MARY STUDDIFORD (*Family practice social worker*): Concerns that come to mind when women with young children are hospitalized are bonding and child care. Many times these issues interfere with patient's compliance toward hospitalization. Mothers who are admitted, leaving an infant or young child at home, may feel inadequate because they are unable to care for their child. A certain degree of resentment toward the caretaker can occur as well as guilt for leaving a child or children at home.

Another recurring theme for women, particularly those with children aged under three years, is the fear that their children won't recognize them

when they are reunited. Arrangements can be made during a lengthy hospitalization to enable the entire family to get together in a quiet corner of the lobby, waiting room, lounge, or even the patient's room.

It is common for women with dependent children to not have anyone who can provide child care, particularly for single parents or families with no relatives in the area. Social workers can help make child care arrangements. When family members are available, but will agree to help only if paid, we can arrange for the county Department of Social Services to reimburse that individual. We can also arrange for homemaker services to provide care in the home to supplement what the family can provide.

In those instances where there doesn't appear to be any alternative, parents have consented to place their children in foster care. Unfortunately, foster care carries negative implications because so many children have been placed as a result of child abuse. One of the advantages is that, when necessary, foster care can be arranged in a matter of hours. Many women would prefer to leave their children with an outside agency than depend on friends or relatives who may not be reliable, and there is never any trouble getting the children out of foster care when it is no longer required.

KATHY CAVANAUGH (*Family practice nurse practitioner*): Do the foster parents bring the children to see the admitted parent?

MARY STUDDIFORD: Sure, and relatives are

Continued on page 358

ALDOMET® (METHYLDOPA) [MSD]

ALDOMET® Ester HCl (METHYLDOPATE HCl) [MSD]

Tablets, containing 125, 250, or 500 mg methyldopa. Oral Suspension, containing 250 mg methyldopa per 5 ml and alcohol 1%, with benzoic acid 0.1% and sodium bisulfite 0.2% added as preservatives. Injection for intravenous use, containing per 5 ml: methyldopate hydrochloride 250.0 mg; inactive ingredients—citric acid anhydrous 25.0 mg, disodium edetate 2.5 mg, monothioglycerol 10.0 mg, sodium hydroxide to adjust pH, and methylparaben 7.5 mg, propylparaben 1.0 mg, and sodium bisulfite 16.0 mg added as preservatives.

Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis; if previous methyldopa therapy has been associated with liver disorders (see Warnings); hypersensitivity to any component, including sulfites (see Precautions).

Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions. With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between 6 and 12 months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood. At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at 6 and 12 months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstated. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first 3 weeks of therapy, occasionally with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first 2 to 3 months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first 6 to 12 weeks of therapy or whenever an unexplained fever occurs. If fever, abnormalities in liver function tests or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstated in such patients. Rarely, a reversible reduction of the white blood cell count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur. Patients should be followed carefully to detect side reactions or unusual manifestations of drug idiosyncrasy.

Pregnancy and Nursing: Use of any drug in women who are or may become pregnant or intend to nurse requires that anticipated benefits be weighed against possible risks; possibility of fetal injury or injury to a nursing infant cannot be excluded. Methyldopa crosses the placental barrier, appears in cord blood, and appears in breast milk.

Precautions: Should be used with caution in patients with history of previous liver disease or dysfunction (see Warnings). Sulfites have been reported to cause severe allergic reactions in certain susceptible individuals, particularly patients with asthma. Oral Suspension ALDOMET and Injection ALDOMET Ester HCl contain sodium bisulfite. Tablets ALDOMET contain no sulfites. Methyldopa may interfere with measurement of: urinary uric acid by the phosphotungstate method, serum creatinine by the alkaline picrate method, and SGOT by colorimetric methods. A paradoxical pressor response has been reported with intravenous use. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, falsely high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. It is important to recognize this phenomenon before a patient with a possible pheochromocytoma is subjected to surgery. Methyldopa is not recommended for patients with pheochromocytoma. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Stop drug if involuntary choreoathetoid movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has recurred after dialysis in patients with methyldopa because the drug is removed by this procedure.

Adverse Reactions: *Nervous System/Psychiatric:* Sedation, headache, asthenia or weakness, usually early and transient; dizziness, lightheadedness, symptoms of cerebrovascular insufficiency, paresthesias, parkinsonism, Bell's palsy, decreased mental acuity, involuntary choreoathetoid movements; psychic disturbances, including nightmares and reversible mild psychoses or depression. *Cardiovascular:* Bradycardia, prolonged carotid sinus hypersensitivity, aggravation of angina pectoris. Paradoxical pressor response with intravenous use. Orthostatic hypotension (decrease daily dosage). Edema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyldopa if edema progresses or signs of heart failure appear.) *Digestive:* Nausea, vomiting, distention, constipation, flatulence, diarrhea, colitis, mild dryness of mouth, sore or "black" tongue, pancreatitis, sialadenitis. *Hepatic:* Abnormal liver function tests, jaundice, liver disorders. *Hematologic:* Positive Coombs test, hemolytic anemia. Bone marrow depression, leukopenia, granulocytopenia, thrombocytopenia. Positive tests for antinuclear antibody, LE cells, and rheumatoid factor. *Allergic:* Drug-related fever, lupus-like syndrome, myocarditis, pericarditis. *Skin:* Rash as in eczema or lichenoid eruption; toxic epidermal necrolysis. *Respiratory:* Nasal stuffiness. *Metabolic:* Rise in BUN. *Urogenital:* Breast enlargement, gynecomastia, lactation, amenorrhea, impotence, decreased libido. *Endocrine:* Hyperprolactinemia. *Musculoskeletal:* Mild arthralgia, with or without joint swelling, myalgia.

Note: Initial adult oral dosage should be limited to 500 mg daily in divided doses when given with antihypertensives other than thiazides. Tolerance may occur, usually between second and third months of therapy; increased dosage or adding a diuretic frequently restores effective control. Patients with impaired renal function may respond to smaller doses. Syncope in older patients may be related to increased sensitivity and advanced arteriosclerotic vascular disease; this may be avoided by lower doses.

For more detailed information, consult your MSD Representative or see Prescribing Information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, PA 19486

MSD
MERCK
SHARP &
DOHME

POSTPARTUM PULMONARY EMBOLISM

Continued from page 355

also strongly encouraged to visit the kids.

DR. NOVAK: Are there any additional questions?

DR. JAMES MARRON (*Assistant Professor, Department of Family Practice*): Where was the site of the thrombosis?

DR. ENDERS: We don't know. On the first admission, we assumed it was of pelvic origin, so did not do any investigating. On the second admission, we did a phleborheogram, and it was negative. We elected not to do a venogram. We did do an echocardiogram to look for a possible thrombosis in the right ventricle. In addition, we wanted to confirm our suspicion of mitral valve prolapse.

QUESTION FROM THE AUDIENCE: Do patients with mitral valve prolapse have a higher incidence of pulmonary emboli?

DR. ENDERS: I don't think so. I am not aware of any such association. On examination she had an intermittent click and a systolic murmur, and my suspicion of mitral valve prolapse was confirmed on the echocardiogram.

DR. NOVAK: I want to thank all of you for a very interesting and informative discussion.

References

1. Platzker AC, Lew CD, Stewart D: Drug administration via breast milk. *Hosp Pract*, Sept 1980, p 122
2. Bell WR, Simon TL: Current status of pulmonary thromboembolic disease. *Am Heart J* 1982; 103:239-262
3. Vorherr H: Puerperium: Management of problems and complications. In Gerbie AB, Sciarra JJ (eds): *Gynecology and Obstetrics*. Hagerstown, Md, Harper & Row, 1980, p 22
4. Hull R, Delmore T, Carter C, Hirsh J, et al: Adjusted subcutaneous heparin versus warfarin sodium in the long-term treatment of venous thrombosis. *N Engl J Med* 1982; 306:189-194
5. Orme ML, Lewis PJ, Swiet MDe, Serlin MJ, et al: May mothers given warfarin breast-feed their infants? *Br Med J* 1977; 1:1564-1565
6. Bell WR, Meek AG: Guidelines for the use of thrombolytic agents. *N Engl J Med* 1979; 301:1266-1270
7. Urokinase Pulmonary Embolism Trial Study Group: Urokinase streptokinase embolism trial: Phase 2, results. *JAMA* 1974; 229:1606-1613