Tanger disease (TD) is characterized by a deficiency or absence of high-density lipoprotein (HDL) and is inherited in an autosomal recessive pattern. Heterozygosity of allelic expression presents clinically as deficient HDL levels, whereas homozygosity presents as absent or nearly critically low HDL levels. The typical presentation of clinical signs includes enlarged, orange tonsils, and liver and heart disease. Tanger disease is rarely described in the anesthetic literature. Appropriate perioperative care, aimed specifically at the condition and any of its manifestations, is essential for optimal management by the clinical anesthesiologist. This topic was identified by committee as required knowledge.

Lesson 239 was reviewed by Elizabeth A.M. Frost, MD, Department of Anesthesia, Mount Sinai School of Medicine, New York, NY.

TARGET AUDIENCE
Anesthesiologists

NEEDS STATEMENT
Tanger disease is an autosomal recessive disorder with systemic effects that can influence the anesthetic course of patients with the disease. The condition, however, is rarely described in the anesthetic literature. Appropriate perioperative care, aimed specifically at the condition and any of its manifestations, is essential for optimal management by the clinical anesthesiologist. This topic was identified by committee as required knowledge.

LEARNING OBJECTIVES
At the end of this activity, the participant should be able to:
1. Summarize the special anesthetic problems presented by the patient with Tanger disease (TD).
2. Describe the systemic changes and symptoms associated with TD.
3. List the complications associated with TD.
4. Outline the genetic factors associated with TD.
5. Construct a differential diagnosis.
6. Present an anesthetic and analgesic plan for the patient.
7. Cite the incidence of the disease.
8. Anticipate, recognize, and manage likely perioperative complications.
9. Anticipate, recognize, and manage likely perioperative complications.
10. Use appropriate additional medical consultation in the perioperative management of patients with TD.

CASE HISTORY
A 14-year-old boy presented to the preanesthetic clinic for evaluation before undergoing a tonsillectomy. On examination, the oral surgeon and anesthesiologist noted that the patient’s tonsils were covered with yellow-orange streaks. The patient’s mother reported that her son had attacks of diarrhea many times per month. The physical examination findings were positive for hepatomegaly and decreased sensation to pinprick in the distal upper extremities. Blood test results were essentially normal except for decreased levels of high-density lipoprotein.

PREANESTHETIC ASSESSMENT
Elizabeth A.M. Frost, MD, who is the editor of this continuing medical education series, is Clinical Professor of Anesthesiology at Mount Sinai School of Medicine in New York City. She is the author of Clinical Anesthesia in Neurosurgery (Butterworth-Heinemann, Boston) and numerous articles. Dr. Frost is also past president of the Anesthesia History Association and former editor of the journal of the New York State Society of Anesthesiologists, Sphere. She is editor of the book series based on this CME program, Preanesthetic Assessment, Volumes 1 through 3 (Binkhauser, Boston) and 4 through 6 (McMahon Publishing, New York City).

A COURSE OF STUDY FOR AMA/PRA CATEGORY 1 CREDIT
1) Read this article, reflect on the information presented, then complete the lesson quiz and course evaluation. Return it to Mount Sinai School of Medicine, Department of Anesthesia, before March 31, 2006. (AMA-PRA credit is not valid past this date.)
2) You must achieve a score of 70% or better to earn CME credit.
3) The estimated time to complete this activity is 2 hours.

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Mount Sinai School of Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCMED) to provide continuing medical education for physicians.

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### Structure of ABCA1

The typical ABCA1 transporter consists of 2 transmembrane domains and 2 nucleotide-binding domains encoded by a single polypeptide. The structural hallmark of the ABCA subfamily is a stretch of hydrophobic amino acids thought to span the membrane within the putative regulatory domain. Up to now, 12 ABCA-encoding genes have been identified, but only 4 ABCA transporters have been fully characterized.

### Mechanism of Action of ABCA1

The function of protein ABCA1 represents the initial and rate-controlling step in the reverse cholesterol transport pathway. Because cholesterol is an integral and necessary membrane component, it is highly likely that ABCA1 targets specific pools of excess, abundant cholesterol molecules for secretion, although the exact mechanisms involved are unknown. Currently, some studies have shown that the interaction of apolipoproteins with cholesterol-loaded cells stimulates the translocation of free cholesterol away from intracellular esterifying enzymes to sites accessible to apolipoproteins.

Another possibility is that ABCA1-containing vesicles travel to intracellular lipid deposits, where ABCA1 pumps lipids into the vesicle lumen, and the vesicles transport the lipid cargo back into the plasma membrane. ABCA1-mediated lipid efflux requires an acceptor apolipoprotein containing an amphipathic helix, such as apo A-I, apo A-IV, or apo E. ABCA1 activity affects membrane morphology by flipping phospholipid to the outer leaflet; active ATPase is essential for apo A-I binding to the cell surface. These findings have led to the idea that apo A-I binds to a region of the membrane disturbed by ABCA1—a conclusion supported by the different lateral mobilities of ABCA1 and apo A-I on the cell surface. Evidence exists for a direct interaction between ABCA1 and the acceptor. Apo A-I crosslinks to ABCA1; mutations in the extracellular loops that abolish cholesterol efflux also abolish crosslinking between the 2 molecules. The terminal helix 10 of apo A-I is necessary for binding; there is a correlation between cholesterol efflux and apo A-I binding. Thus, a sequence can be envisaged in which ATP-dependent ABCA1 activity disturbs the membrane and allows apo A-I to bind through helix 10. If then diffuses until it directly interacts with ABCA1, when the productive complex lipids the apo A-I to form nascent HDL disc. ABCA1 transports both phospholipid and cholesterol, and thus confers a greater degree of specificity.

Finally, the lipids could be directly transferred to the tethered acceptor. This explanation is intuitively more plausible, but the precise means of transfer will probably not be defined until the manner in which the transporter acts has been elucidated.

The binding and hydrolysis of ATP flip the substrate from the inner leaflet of the membrane either directly to the outer leaflet or into the outer medium, from which it transfers to an acceptor or back into the outer leaflet. More detailed structures of Escherichia coli transporters have shown bundles of transmembrane helices either touching at the outer surface or touching through cytoplasmic domains. Thus, a tilting mechanism of action has been proposed: The helices bind the substrate when open at the cytoplasmic side and then release it to the outside when the V-shaped structure is inverted. Evidence supporting this mechanism was obtained by the use of nometabolized compounds to trap the ATPase cycle at different stages to determine structure and substrate affinity. The binding of ATP produces marked conformational changes in the transmembrane domains and a reduction in affinity—changes that are reversed on hydrolysis of ATP, with release of adenosine diphosphate (ADP) and phosphate.

### Regulation of ABCA1 Gene Expression

The ABCA1 gene is tightly regulated by the cholesterol status of the cell. Cholesterol efflux is stimulated when macrophages are loaded with cholesterol. This effect of cholesterol is mediated by the stimulation of gene transcription by the liver X receptor (LXR), a nuclear hormone receptor that is activated by oxysterol ligands. The human ABCA1 gene has 2 promoters, both of which contain elements that bind LXR. These promoters do not account for the well-known stimulation of cholesterol efflux by cyclic adenosine monophosphate (cAMP), suggesting that there may be many more remote enhancers. ABCA1 activity can also be greatly influenced by post-translational processes. Unsaturated fatty acids and cholesterol can increase ABCA1 degradation, although the pathway involved is not known. ABCA1 contains so-called PGST (Pro-Glu-Ser-Thr) sequences that are required for proteolysis through the calpain pathway. Binding of apo A-I greatly stabilizes ABCA1 by inhibiting calpain-mediated degradation.

### Mutations

Genetic analysis has revealed that TD is due to mutations in both alleles of the ABCA1 gene, whereas familial HDL deficiency is due to a mutation in a single allele. The ABCA1 gene—located on chromosome 9 (9q31)—contains 50 exons. Since the ABCA1 gene was found to be responsible for TD, several causative mutations have been identified in affected individuals. TD has been linked to mutations on chromosome 9q22-31, which is the location of the gene encoding human ABCA1. Familial HDL deficiency (FHD) is a more common cause of low HDL levels. The FHD locus has now been mapped to the same genomic region as the TD locus. Mutations in TD1 were detected in both cases (TD and FHD), indicating that TD and FHD are allelic. Furthermore, inactivation of the ABCA1 gene in ABCA1 knockout mice resulted in a decrease of plasma cholesterol and phospholipids and the virtual absence of plasma HDL.

### Pathogenesis

**ABCA1 Transgenic Mice**

The best model in which to determine the existence of a single mutation for a disease is the transgenic mouse. Many different mutations lead to a defective ABCA1 transporter, and several have been discovered recently. Knockout animals show the expected absence of HDL and no increase in atherosclerosis. Affected patients show a decrease in plasma LDL concentration, which has also been seen in ABCA1 knockout mice. Knocking out ABCA1 in macrophages of both apo E-null and LDL receptor-null mice enhances the development of atherosclerosis. Thus, it seems that the ABCA1-mediated efflux of cholesterol can reduce atherosclerosis. This benefit, however, can be overcome by various proatherogenic effects.

The bulk of pre-HDL is probably formed in the liver—a supposition based on several observations: ABCA1 is highly expressed in the liver, the protein is present on the basolateral surface of hepatocytes, and increased hepatic concentrations of cholesterol have been observed in a patient with TD. More direct evidence comes from mice with specific overexpression of ABCA1 in the liver. A significant increase in plasma levels of mature lipoprotein HDL was found in these animals. Although no net decrease in liver cholesterol content was noted, there was a compensatory increase in the expression of 3-hydroxy-3-methylglutaryl-CoA reductase and LDL receptors to make up for the loss of cholesterol. Thus, hepatic ABCA1-mediated cholesterol efflux contributes to the generation of mature HDL and the regulation of liver cholesterol levels. It provides a further pathway for the removal of cholesterol from the liver and allows the 2 pathways trafficking of HDL cholesterol to and from peripheral tissues.

### Role of ABCA1 in the Formation of HDL

Apo A-I-mediated cholesterol efflux involves the binding of apo A-I to the plasma membrane via its C-terminal and requires cellular ABCA1 activity. Apo A-I also stimulates the secretion of apo E from macrophage foam cells. Apo A-I stimulates the secretion of apo E independently of both ABCA1-mediated cholesterol efflux and lipid binding by its C-terminus. ABCA1 gene expression is decreased in diabetic mice. In humans, the presence, even within normal range, of a glycosylated hemoglobin, HbA1c, predicted future coronary heart disease events. Leukocyte ABCA1 gene expression is inversely associated with indices of glycaemia in normoglycemic men. Increased fasting or postprandial triglyceride levels frequently accompany low HDL cholesterol levels and can add to the risk for a vascular event. In addition, postprandial

| Table 1. Differential Diagnosis of Tangier Disease |
|---|---|
| **Tangier disease** |
| *Enlarged tonsils streaked with yellow-orange (80% of cases)* |
| Decreased HDL |
| Decreased apo A-I |
| Hepatosplenomegaly |
| Peripheral neuropathy |
| Orange-brown mucosal spots in colon and rectum |

| **Primary hypoalphalipoproteinemia** |
| HDL level below 10th percentile, normal cholesterol and triglycerides |

| **Familial LCAT deficiency** |
| Corneal opacification in young adulthood |
| Low HDL levels with variable hypertriglyceridemia |
| Anemia, progressive proteinuria, renal insufficiency (complete form) |
| *Also known as ‘isolated low HDL’* |

| **Abetalipoproteinemia** |
| Pigmented retinopathy leading to loss of night and color vision |
| *Sporocerebellar degeneration* |
| Total cholesterol and triglyceride levels decreased; no VLDL or apo B |
| *Decreased DTRs; decreased vibratory sense, proprioception in distal lower extremities* |
| Cerellel signs: dysmetria, ataxia, spastic gait |

| **Familial apo A-I deficiency and structural apo A-I defects** |
| Acquired corneal opacities |
| Possible cutaneous or planar xanthomas |
| Possible nearly absent HDL |
| *Complete deficiency of apo A-I* |

*These symptoms and concepts are the most important for a correct diagnosis.*
Obtain preoperative platelet and reticulocyte count
Investigate for possible complications of airway management

<table>
<thead>
<tr>
<th>Complication</th>
<th>Management Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>Obtain preoperative platelet and reticulocyte count</td>
</tr>
<tr>
<td>Consider treatment with 1-desamino-8-arginine vasopressin</td>
<td></td>
</tr>
<tr>
<td>*Caution with medications affecting coagulation; consider hematology consult</td>
<td></td>
</tr>
<tr>
<td>Neupathy</td>
<td>Avoid succinylcholine (may induce hyperkalemia)</td>
</tr>
<tr>
<td>Avoid regional anesthesia</td>
<td>Monitor for exaggerated response to nondepolarizing muscle relaxants</td>
</tr>
<tr>
<td>Enlarged tonsils</td>
<td>Investigate for possible complications of airway management</td>
</tr>
<tr>
<td>*Caution with midazolam and 50% N₂O</td>
<td></td>
</tr>
</tbody>
</table>

Both types are characterized by particularly low plasma levels of HDL cholesterol and variable hyperglycemia. A diagnosis of LCAT deficiency, rarely made in childhood, is suspected in cases of corneal opacification, renal insufficiency, or an incidentally discovered low HDL cholesterol level. The diagnosis can be confirmed by specialized laboratories based on quantification of LCAT and cholesterol esterification activity in the plasma. Remarkably, despite extremely low levels of HDL cholesterol and apo A-I, the risk for premature atherosclerotic cardiovascular disease does not appear to be increased in either complete or partial LCAT deficiency.

Abetalipoproteinemia

Abetalipoproteinemia is a rare autosomal recessive disease characterized by the malabsorption of fat, spinocerebellar degeneration, and pigmentary retinopathy. The biochemical hallmark of this disease is the strikingly abnormal profile of plasma lipids and lipoproteins. Total cholesterol and triglyceride levels are extremely low, and there are no detectable levels of plasma chylomicrons, very low-density lipoprotein (VLDL), or LDL. Furthermore, apo B is completely absent from the plasma. This disease is caused by a mutation in the gene for microsomal triglyceride transfer protein, which mediates the intracellular transport of membrane-associated chylomicrons in enterocytes and VLDL in hepatocytes. The most prominent and debilitating clinical manifestations of abetalipoproteinemia are neurologic; these usually begin in the second decade. The first sign of disease is usually the loss of deep tendon reflexes, followed by decreased vibratory and proprioceptive senses in the distal lower extremities, in addition to cerebellar signs such as dysmetria, ataxia, and spastic gait. The clinical outcome is variable, but the result in untreated patients is often severe ataxia and spasticity by the third or fourth decade. Severe effects on the central nervous system—the ultimate cause of death in most patients—often develop by the fifth decade or earlier.

Patients with abetalipoproteinemia also acquire a progressive pigmentary retinopathy. The presence of both spinocerebellar degeneration and pigmentary retinopathy in this disease may result in a misdiagnosis of Friedreich's ataxia. The first ophthalmic symptoms are decreased night and color vision. Daytime visual acuity usually deteriorates inexorably to virtual blindness by the fourth decade.

Most of the clinical symptoms of abetalipoproteinemia are the result of defects in the absorption and transport of fat-soluble vitamins, especially vitamin E. Vitamin E is transported from the intestine to the liver, then “repackaged” in the liver and incorporated into the VLDL particles as a specific lipid, the tocopherol-binding protein. In the circulation, VLDL is converted to LDL, and vitamin E is transported by LDL to peripheral tissues and delivered to cells via the LDL receptor. Patients with abetalipoproteinemia are markedly deficient in vitamin E.4

Familial Lechithin:Cholesterol Acyltransferase Deficiency

Familial LCAT deficiency is related to an efflux of unesterified cholesterol from cells to HDL. Two general types of genetic LCAT deficiency have been described in humans: complete and partial (fish eye disease). Progressive corneal opacification in young adulthood is characteristic of both types. In addition, complete (classic) LCAT deficiency—but not partial deficiency—is characterized by anemia, progressive proteinuria, and renal insufficiency in young adulthood.

Both types that present the biosynthesis of apo A-I protein may result in a virtual absence of plasma HDL. These extremely rare patients present with acquired corneal opacities and occasionally cutaneous or planar xanthomas. The risk for premature cardiovascular disease in patients with apo A-I deficiency is increased, but the onset of symptoms in such patients has varied from the third to the seventh decade. By contrast, mutations of the apo A-1 gene that permit the secretion of a mutant apo A-1 protein are not generally associated with premature coronary artery disease. A few apo A-I gene mutations have been described in association with systemic amyloidosis, and mutant apo A-1 protein has been found as a component of amyloid plaque.6

Treatment

There is no definitive treatment for TD; in recent years, however, numerous studies have shown promising results of certain treatments for this illness, and many other studies have shown some efficacy. Attention has focused on ABCA1. Since identification of the gene, efforts have been increased to produce drugs that stimulate the defective ABCA1 transporter to lower dangerous accumulations of cholesterol in the macrophages of atherosclerotic lesions.21,22 Study results also indicate that certain oysteroids—eg, 22(R)/hydroxysterol—can increase ABCA1 expression by serving as an agonist of LXR. Another mechanism that may lead to the same expression involves the inhibition of Rho GTP-binding proteins. In both studies, the increased expression and promoter activity of ABCA1 protein was indicated.23

ABCA1 uses the CAMP/protein kinase A pathway for apo A-I lipidation—a necessary step for the HDL reverse cholesterol transport pathway. In one trial, patients with TD received 8-bromo-cAMP and forskolin, a CAMP regulator. With neither treatment was ABCA1 phosphorylated to enter the arterial wall. Severe effects on the central nervous system—the ultimate cause of death in most patients—often develop by the fifth decade or earlier.

Recent studies have found huge amounts of Niemann-Pick C1 (NPC1) protein in the cholesterol of late endosomes trying to enter the reverse cholesterol pathway in affected patients; this may impede vitamin transport between tissues and lipid oxidation. However, these deficiencies can be treated by raising HDL levels because HDL may promote eicosanoids through ABCA1-dependent and-independent processes.38

By hindering eicosanoid, nonfunctional ABCA1 protein may impede vitamin transport between tissues and lipid oxidation. However, these deficiencies can be treated by raising HDL levels because HDL may promote eicosanoids through ABCA1-dependent and-independent processes.38

Recent studies have found huge amounts of Niemann-Pick C1 (NPC1) protein in the cholesterol of late endosomes trying to enter the reverse cholesterol pathway in affected patients; this may impede vitamin transport between tissues and lipid oxidation. However, these deficiencies can be treated by raising HDL levels because HDL may promote eicosanoids through ABCA1-dependent and-independent processes.38
the ramifications associated with the illness. However, for some of the same study came a promising insight: Adenosinemediat-
ed ABCA1–green fluorescent protein allowed NPC1-containing cholesterol to be converted, thereby restoring the proper reverse cholesterol pathway.27 This discovery holds great promise for the treatment not only of TD but also of other cardio-
vacular diseases.

Treatment of Low HDL Levels in Patients With TD
In a study by Meco and colleagues, 16 patients with TD, coronary artery disease, and impaired flow-mediated endothelium-
dependent dilation were treated with 400 mg of bezafibrate daily for 6 months. Endothelial function improved with a simul-
taneous increase in levels of both HDL and apo A-I.28

Thrombocytopenia
Patients with TD can present with thrombocytopenia. A history of easy bruising or bleeding should prompt an exami-
nation of its cause. Preoperative platelet and reticulocyte counting is recommended for these patients.

Management of the Case
The patient’s tonsillectomy was postponed for 1 day after further testing was conducted. The patient’s airway was evaluated by an ear, nose, and throat surgeon and a senior anesthesiologist for potential complications of intuba-
tion; none were found. Echocardiography findings revealed a normal ejection fraction of 65%, with no organic heart murs, regurgitation, or gallops. Liver function tests were ordered, and the results were within normal limits. A slightly prolonged prothrombin time suggested mildly abnormal coagulability. The operative plan included the administra-
tion of fentanyl, desflurane, oxygen, air, and enoxaparin. The surgery was scheduled for the following day and was performed without complications; the patient returned home in the afternoon.

Summary
Current, no cure for TD is known; therefore, sympto-
matic treatment is the therapeutic mainstay. An under-
standing of the mechanisms involved in ABCA1 trans-
porter dysregulation is important for success in treat-
ing these patients. The disease is often diagnosed in childhood owing to characteristic tonsillar enlargement; however, a thorough review of symptoms is required to identify associated liver, heart, nervous system, and vascu-
lar complications. The evaluation of preoperative symp-
toms and the success of regional blocks can be confounded by the presence of ongoing neuropathy. How-
ever, with careful monitoring, several anesthetic regimens have been used successfully.

References
19. Alin J, Rosier M, Funke H, et al. Tangier disease is caused by mutations in the gene encod-
27. Alin J, Rosier M, Funke H, et al. Tangier disease is caused by mutations in the gene encod-
Lesson 239: Post-test

Select the single-letter response that most correctly answers the question or completes the sentence.

1. Tangier disease (TD) is inherited in which of the following patterns:
   a. autosomal dominant
   b. autosomal recessive
   c. X-linked
   d. maternal

2. Definitive treatment of patients with TD includes which of the following:
   a. 12 months of corticosteroids
   b. low-dose aspirin plus statins
   c. niacin therapy to raise HDL levels
   d. No treatment exists.

3. Mutations in the gene encoding ABCA1 transporter result in pathology because ______.
   a. ABCA1 mediates the efflux of excess cellular cholesterol to apo A-I, leading to the formation of HDL
   b. ABCA1 directly decreases peripheral LDL cholesterol
   c. ABCA1 upregulates enzymes necessary for proper liver function
   d. none of the above

4. Tonsils streaked with yellow-orange are present in what percentage of patients with TD:
   a. Percentage varies by race.
   b. 40%
   c. 80%
   d. 100%

5. The differential diagnosis for TD includes ______.
   a. primary hypophysial hypoproteinemia
   b. familial LCAT deficiency
   c. familial apo A-I deficiency
   d. all of the above

6. The primary vascular pathology in TD is ______.
   a. endothelial hypertrophy due to lack of ABCA1
   b. calcification secondary to lack of ABCA1
   c. inflammation of medium-sized vessels secondary to lack of ABCA1
   d. atherosclerosis secondary to lack of ABCA1

7. The mechanism of ABCA1 and lipidation uses ______.
   a. a tyrosine kinase pathway
   b. a cAMP/protein kinase A pathway
   c. a voltage-regulated channel pathway
   d. sodium/potassium ion transport

8. Drugs shown to improve endothelial function in patients with TD include ______.
   a. ACE inhibitors
   b. bezafibrate
   c. gemfibrozil
   d. cholestyramine

9. Prolonged bleeding in patients with TD has been controlled by ______.
   a. transfusion
   b. erythropoietin infusion
   c. administration of 1-desamino-8-d-arginine vasopressin
   d. avoidance of aspirin or other anticoagulants 2 weeks before surgery

10. Intubation may be complicated for the following anatomic reason in patients with TD:________.
    a. laryngeal spasm
    b. hypertrophic tongue
    c. enlarged tonsils
    d. narrow trachea

11. Were any parts of the lesson unsatisfactory or inappropriate?________.
    a. Yes
    b. No
    c. Not Applicable

12. What topics would you like to see included in future programs?________.

13. Were you able to call the CME office at (212) 241-4441 or e-mail Josephine.Greene@mssm.edu if you required administrative assistance for a question about content?________.
    a. Yes
    b. No
    c. Not Applicable

14. If you were designing the program, would you modify the structure? If so, how?________.

15. Are you likely to make changes in your work setting or clinical practice as a result of this CME activity?________.
    a. Yes
    b. No
    c. Not Applicable

Please return response forms to:

Josephine Greene
Mount Sinai School of Medicine, Department of Anesthesia
One Gustave L. Levy Place, Box 1010, New York, NY 10029

Please type or print clearly.

Preanesthetic Assessment of the Patient with Tangier Disease

To receive CME credit, you must complete this form, including the time attestation and evaluation, score ≥70% on the quiz, and return the form with a check for $10 made payable to MSSM-Anesthesia before March 31, 2006, to Mount Sinai School of Medicine, Department of Anesthesia, One Gustave L. Levy Place, Box 1010, New York, NY 10029. Credit will be awarded only for lessons completed with a signed time attestation that are postmarked before the expiration date.

1. a b c d 6. a b c d
2. a b c d 7. a b c d
3. a b c d 8. a b c d
4. a b c d 9. a b c d
5. a b c d 10. a b c d

I certify that I completed this CME activity; the actual time I spent on this activity was:

______ HOURS ______ MINUTES

SIGNATURE______________

Preanesthetic Assessment Course Evaluation

Your frank and considered evaluation will be helpful in improving our CME programs. Your assistance is greatly appreciated.

1. This lesson met the stated objectives.
   a. Strongly Agree
   b. Agree
   c. Disagree
   d. Strongly Disagree

2. This lesson met my expectations.
   a. Strongly Agree
   b. Agree
   c. Disagree
   d. Strongly Disagree

3. This lesson enhanced my knowledge.
   a. Strongly Agree
   b. Agree
   c. Disagree
   d. Strongly Disagree

4. This lesson improved my skills.
   a. Strongly Agree
   b. Agree
   c. Disagree
   d. Strongly Disagree

5. I am satisfied with the content of this lesson.
   a. Strongly Agree
   b. Agree
   c. Disagree
   d. Strongly Disagree

6. The information I gained from this lesson will be applicable to my practice.
   a. Strongly Agree
   b. Agree
   c. Disagree
   d. Strongly Disagree

7. I am satisfied with the content of this lesson.
   a. Strongly Agree
   b. Agree
   c. Disagree
   d. Strongly Disagree

8. This lesson was free of promotional and commercial bias.
   a. Strongly Agree
   b. Agree
   c. Disagree
   d. Strongly Disagree

9. The format used for this lesson was appropriate.
   a. Strongly Agree
   b. Agree
   c. Disagree
   d. Strongly Disagree

10. Which parts of the lesson were most useful?

11. Were any parts of the lesson unsatisfactory or inappropriate? If so, which?

12. What topics would you like to see included in future programs?

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   b. No
   c. Not Applicable

14. If you were designing the program, would you modify the structure? If so, how?

15. Are you likely to make changes in your work setting or clinical practice as a result of this CME activity?
   a. Yes
   b. No
   c. Not Applicable

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