Thrombophilia

**Definition:** Thrombophilia is a hereditary or acquired disorder predisposing to thrombosis. The following two tables outline thrombophilic disorders that are acquired and those that are familial.

<table>
<thead>
<tr>
<th>Familial thrombophilia</th>
<th>Acquired thrombophilia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic or recurrent DVT</td>
<td>Malignant neoplasm</td>
</tr>
<tr>
<td>Superficial or deep thrombosis</td>
<td>Myeloproliferative disorder</td>
</tr>
<tr>
<td>Arterial thrombus (stroke/other)</td>
<td>Oral contraceptives</td>
</tr>
<tr>
<td>Pregnancy complications</td>
<td>Estrogen replacement or tamoxifen</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>Intravascular coagulation</td>
</tr>
<tr>
<td>Fetal growth retardation</td>
<td>Lupus anticoagulant/anticardiolipin antibody</td>
</tr>
<tr>
<td>Recurrent fetal loss</td>
<td>Pregnancy – post partum state</td>
</tr>
</tbody>
</table>

**Who should be tested?**
- Patients with venous thromboembolism (without malignancy or vascular catheters)
- Family history of venous thrombosis
- Disorders of familial thrombophilia (see above)

**What tests to order?** Assays are given in recommended order of testing given the statistical likelihood if the disorder. Clinical judgment is necessary for all lab testing.
- Factor V Leiden [Activated Protein C (APC) resistance]
- Lupus anticoagulant and anticardiolipin antibody
- Prothrombin 20210 G mutation
- Assays for DIC; fibrinogen and D-dimer
- Plasma homocysteine
- Assays for Protein C, protein S and antithrombin III

**When to test?**
- Delay two or three months after acute thrombosis or delivery. This interval allows all acute phase reactants to return to baseline.
- Heparin can lower antithrombin III levels
- Coumadin lowers levels of protein C and S
- Direct testing for Factor V Leiden and Prothrombin 20210 is unaffected by anticoagulant therapy and done at any time

**How to manage patients with familial thrombophilia?** Recommendations of the College of American Pathologists consensus conference (2002, in press)
- Asymptomatic patients should receive antithrombotic prophylaxis when exposed to thrombotic risk factors (e.g., surgery, trauma etc.)
- Screen women with a known family history prior to commencing oral contraceptive or hormone replacement therapy

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• Anticoagulant prophylaxis is indicated in pregnancy and puerperium.
• Long term antithrombotic therapy not recommended for asymptomatic factor V Leiden carriers

Reference


Cytologic Screening of the Anal Canal

Homosexual and bisexual men and women infected with human immunodeficiency virus (HIV) are at a significantly increased risk for the development of human papillomavirus (HPV) mediated anal neoplasia including the spectrum of condyloma acuminata to squamous cell carcinoma. Non-HIV infected men and women who engage in receptive anal intercourse are also at increased risk. This non-HIV infected cohort is estimated to have an incidence of anal carcinoma of 35/100,000 which is approximately the same incidence of cervical cancer suffered by women before the advent of routine cervical Pap smear screening. The HIV positive cohort is estimated to have at least twice the incidence of anal carcinoma compared to the HIV negative cohort. (1)

Cytologic screening of the anal canal in these at risk groups has been recommended as a means to detect anal neoplasia in early stages of development analogous to cervical Pap smear screening in women. (2) The recommended sampling procedure includes first placing the patient in either a knee to chest or lateral position. The anus is gently spread open and then, without lubrication, a water moistened Dacron® swab is inserted at least 3-4 cms above the level of the sphincter. Using the sphincter as a fulcrum, the swab is rotated 360 degrees while maintaining firm pressure against the anal wall. The swab is then extracted and swished thoroughly in either SurePath® cytology fixative or ThinPrep® cytology fixative. (3) The cytology laboratory will then process and screen the slide using diagnostic criteria very similar to that used for cervical Pap smear reporting in women.

Abnormal anal cytology has been documented in 19-30% of homosexual/bisexual men in the general population. A recent study of these men, including both HIV+ and HIV- individuals, presenting for surgical management of anal condyloma and noncondylomatous benign disease discovered a 93% prevalence of abnormal anal cytology including several cases of clinically unexpected squamous cell carcinoma. (1). 60% of the abnormal cytologies were confirmed as high-grade squamous intraepithelial lesions (carcinoma-in-situ) and 3% as squamous cell carcinoma. Based on clinical examination alone, only 2% of these patients had been suspected of having anything worse than condyloma.

An algorithm for the screening and evaluation of these patients has been recommended. (1,3) Initially all HIV+ women as well as both HIV+ and – homosexual/bisexual men should be screened. HIV+ individuals with normal cytology should have annual repeat screening. HIV- individuals with normal cytology could be re-screened every two-three years. Any individual with abnormal cytology should be examined using high-resolution anoscopy (HRA), analogous to colposcopy, with abnormal areas biopsied. Squamous cell carcinomas are treated with established protocols and areas of high-grade dysplasia ablated or excised using electrocautery, cryotherapy or laser.

Cytologic screening of the anal canal in this patient population has not yet been established as a standard of care (3) but has been shown to be useful in detecting clinically unsuspected disease at an early treatable stage and thus to offer cost effective life expectancy and quality of life benefits. (1,3,4,) Any attempt to establish a screening program in this area should include the development of a follow-up/treatment infrastructure including individuals trained in high-resolution anoscopy and localized excision of affected areas.
References


Work-up of Nosocomial Diarrhea (Flushing $$$ Down the Toilet)

Hospital acquired or nosocomial diarrhea is defined as acute diarrhea beginning after the third day of admission. Patients who acquire diarrhea in the hospital have different etiologies than those with community acquired diarrhea. Inpatient cases are often noninfectious, and those related to an infectious etiology are most commonly caused by Clostridium difficile, Candida, and in pediatric cases, rotavirus. Routine stool culture pathogens (Shigella, Salmonella, Yersinia, and Campylobacter) are responsible for less than 1% of cases of nosocomial diarrhea. Similarly, nosocomial diarrhea is unlikely to be caused by intestinal parasites detected by ova and parasite examination of stool.

Investigators at the University of Pennsylvania performed a three-year retrospective study on inpatient testing for diarrheal disease. During that period there were 191 positive stool cultures and 90 positive ova and parasite examinations. Only 1 of the positive stool cultures and none of the ova and parasite examinations were from patients who had stool specimens submitted after the third day of hospitalization. Despite the exceedingly low prevalence of positive tests, the workload from this group comprised nearly 50% of the 3000 specimens received each year for stool microbiology.

A study of inpatient ova and parasite examinations ordered at Rex from January to October 2002 showed similar results.

Rex Hospital - Ova and Parasite Examinations (January -October 2002)

<table>
<thead>
<tr>
<th>Ova and parasite stool examination</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>First 3 days in hospital</td>
<td>6</td>
<td>194</td>
</tr>
<tr>
<td>After 3 days of admission</td>
<td>0</td>
<td>43</td>
</tr>
</tbody>
</table>

Furthermore, the 6 “positive” patients harbored organisms that are usually considered to be nonpathogenic, casting further doubt on the utility of this study in inpatients.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Hospital day (1 = day of admission)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blastocystis hominis</td>
<td>2</td>
</tr>
<tr>
<td>Blastocystis hominis</td>
<td>1</td>
</tr>
<tr>
<td>Entamoeba hartmanii</td>
<td>2</td>
</tr>
<tr>
<td>Endolimax nana</td>
<td>1</td>
</tr>
<tr>
<td>Endolimax nana</td>
<td>2</td>
</tr>
<tr>
<td>Endolimax nana</td>
<td>1</td>
</tr>
</tbody>
</table>

Some have proposed that laboratories refuse specimens for stool culture or ova and parasite examination after the third day of admission. With an increasing number of immunosuppressed patients it is recognized that the usual
patterns of infection may not always apply. One guideline from the United Kingdom attempts to take other factors into account in the ordering of stool cultures. They are as follows:

**Criteria for stool culture for enteropathogenic bacteria in adult patients (maximum 3 specimens per patient):**
1. Diarrhea within 72 hours of admission
2. Onset of diarrhea more than 72 hours after admission ONLY IF one of the following applicable:
   - Age 65 years or more AND pre-existing disease causing permanently altered organ function.
   - HIV infection.
   - Neutropenia <0.5 x 10^9/L.
   - Suspected nosocomial outbreak.

From a cost perspective, stool cultures and ova and parasite examinations are labor intensive, and therefore expensive. Estimates vary greatly, but it is clear that a reduction in routine stool cultures and ova and parasite examinations on hospitalized patients would yield a significant cost reduction for hospitals without a compromise in patient care. At Rex we will continue to monitor ova and parasite requests on inpatients after day three of hospitalization.

**Recommendations:** For cases of nosocomial diarrhea fresh stool should be submitted for C. difficile toxin testing. Two stools are recommended on successive days. Well formed stool is not useful as diarrhea should be present. Routine stool cultures and ova and parasite examinations are not recommended

Vincent C. Smith MD

**References**

For further information, call the Laboratory (784-3040). Telephone extensions are: Pathologists’ Direct Line (3201), Sharon Logue (Lab Director 2400), Robin Ivusic (Outreach and Microbiology Lab Manager 3053), Elaine Patterson (Core Lab Manager 3054), Jackie Okoth (Core Lab PM Manager 4248), Diane Young (Anatomic Pathology Manager 3888), Nga Moore (Customer Service Manager 3396), Diane Stephenson (Blood Bank Manager 4767), Justin Hodges (Blood Plan Manager 4750)

Guidelines: Primary Prevention of Cardiovascular Disease and Stroke from Journal Watch

Physician-authored summaries and commentary from the publishers of the New England Journal of Medicine

Posted 11/01/2002

**Summary**

**Sponsoring Organization:** the American Heart Association

**Background and Purpose:** In 1997, the AHA published a brief guide to assist practitioners in reducing cardiovascular risk in their patients without coronary or other atherosclerotic vascular diseases (Circulation 1997; 95:2329). Since then, an array of detailed primary-prevention recommendations for particular conditions and risk factors have been developed.
groups have been published. This 2002 revision provides a framework within which to understand the current, more detailed landscape of primary-prevention recommendations.

1. Blood-pressure recommendations have been expanded to include more stringent targets for patients with renal insufficiency or heart failure (<130/85 mm Hg) and for diabetics (<130/80 mm Hg). The target for others remains <140/90 mm Hg.
2. Aspirin is recommended for people with a 10-year risk for coronary heart disease (CHD) of >/=10%. (Aspirin was not listed as a risk intervention in 1997.)
3. Moderate physical activity of at least 30 minutes is now recommended for most -- if not all -- days of the week (not just 3 to 4 days per week, as in 1997).
4. For weight management, the body-mass index goal has been expanded from 21-25 kg/m² to 18.5-24.9 kg/m².
5. Diabetes management has been added as a risk intervention: Goals are fasting blood glucose <110 mg/dL and hemoglobin A₁c <7%.
6. A recommendation about atrial fibrillation has been added, most notably an anticoagulation target (INR, 2.5).
7. Diet is now mentioned specifically, with a recommendation for fruits, vegetables, grains, fish, legumes, poultry, lean meat, and low-fat dairy items.
8. Smoking cessation remains an important recommendation, but the new guidelines also suggest counseling patients to avoid secondhand smoke.
9. The cholesterol-management recommendations have been strengthened. For people with at least 2 risk factors and 10-year CHD risk of >/=20%, the target LDL level is now <100 mg/dL. Statin therapy is also more liberally recommended.
10. All recommendations for estrogen replacement therapy have been removed from the guidelines.

Comment
These guidelines provide an enormously useful summary of the best ways to reduce cardiovascular risk in patients without CHD. The user-friendly format is particularly suitable for use as a checklist during patient visits.
— Harlan M. Krumholz, MD, SM

Source