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Cover: “Tibetan Singing Bowl & Mallet,” oil on board, by Bill Chisholm, a Rhode Island artist whose most recent solo shows include the Jessica Hagen Gallery, the Marion Art Center, and the Thomas Henry Gallery. Much of his work can be viewed at www.billchisholm.com.
Yawning, or Not Having Enough To Do

A colleague told me that he had just seen a patient who had been bothered by yawning for the past two years and wanted to do something about it. It apparently was not due to any identifiable disorder or medication. It turns out, unbeknownst to my friend, that I had co-authored a case report on yawning in Parkinson’s disease (PD). My report described a man who had suffered from PD for many years and suffered from severe clinical fluctuations, the so-called “on-off” problem. He told me that about two minutes or so before his medications “kicked in” and put him into an “on” phase he would yawn. He otherwise didn’t yawn, and he denied sleepiness. I witnessed this once. He was stuck in a wheelchair, unable to stand and walk; he was stiff, slow, and pretty well frozen in place. He then began to yawn and two minutes later he was dyskinetic but mobile, able to stand up and walk by himself. This had not been described in the literature before, and, although I hadn’t a clue as to what this “meant” in the greater scheme of neurotransmitter physiology, I was sure it meant something.

I later learned that yawning was a very common reaction to one of the standard medications used in Europe for many years to treat PD, apomorphine, but that medication had not yet been tested in the US. When I wrote my article (and I must point out that that little case report attracted more interest than any of the useful observations or studies that I had published) the only thing I knew about yawning was that it was contagious and that it occurred not only when humans are sleepy or bored, but also when they are nervous.

When my friend contacted me recently about his yawner, I did a Pubmed search and was floored to find out how many people had written articles about yawning. There was even articles relating yawning to diseases, drugs and hypothetical physiological mechanisms.

Is yawning so interesting or are there a lot of researchers who are under-employed? There are a few interesting things about yawning. The first is that it is contagious. The second is that yawning is widespread in the animal kingdom and is contagious in some of them. The third is that yawning has been identified in utero. It seems that babies are not susceptible to contagious yawning, at least not from their mothers, which is, I think, a cruel trick on mothers. But most interesting of all, at least to a neurologist, is that some patients with a hemiparesis from a stroke, will raise an otherwise paralyzed arm during a yawn, as an involuntary reflex.

I suspect that yawning has attracted attention simply because it is so universal and yet carries no identifiable benefit. In fact, one can argue that yawning probably causes more trouble than it solves, at least in humans. Certainly the parent of a small, yawning child realizes that the child needs a nap. But just as certainly the teacher of a yawning child realizes that the child’s boredom quotient has outweighed the interest level. Yawns are generally not well received by the person who may be causing the condition. On the other hand, as a neurologist who gives fairly frequent talks, I use the incidence of yawning and myoclonic jerks as an inverse measure of how good a talk I’ve given. No yawns, myoclonic jerks or sleep attacks indicates a good lecture.

I think of the study of yawning in non-human species as being a continuation of “natural philosophy” of the 18th century, perhaps, in some cases using 21st century tools. When one tries to deduce the behavioral consequences or behavioral causes of yawning behavior in non-primate animals, one has trod onto a playground more philosophical than scientific, even if one uses scientific experimental techniques. After all, as the authors argue, it is not at all clear that what looks like a yawn in some species is, in fact, the same thing as a human yawn. One paper defines a yawn as “an extended gap of the mouth followed by a more rapid closure.” I don’t think any of us perceives a crocodile with its mouth open, as yawning. And just as far afield, it is unclear if a bird displaying yawning-type movements, is in fact yawning, and similarly for a fetal human. And what does one make of fish, like Siamese fighting fish, which open their mouths and seem to yawn, although they don’t have lungs to take in air that primates do when yawning?

I suspect that all normal humans yawn, although I don’t know if that’s a fact. Perhaps there are people who never yawn, no matter how tired or bored. Would that have any meaning? What if absence of yawning was associated with some other unusual behavior? To be sure the association was more than chance, we’d need to evaluate a few patients with similar behavior. But then, even if we found a few people with the same sets of unusual behaviors, until we found a genetic or physiological link, any deductions would be speculative, not scientific.

Attempting to draw evolutionary advantages to behaviors may be entertaining and challenging but are unlikely to be good science because we can never control all variables, and the basic driving force of evolution is the random event. Most results of random events are negative, but not all. Occasional events are advantageous. Many are likely to be neutral, and if linked to something advantageous, live on and prosper.

Yawning is more interesting than the palmo-mental reflex or the corniculo-mandibular reflex, but what is the point of a debate on the “meaning” of a yawn? While I like a good argument, does anyone really care?

-- Joseph H. Friedman, MD

Disclosure of Financial Interests

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Who Amongst Us Will Be Selected?

It is early winter of 2011 and influenza is endemic in Providence. Thirty-four youngsters attend a local first grade elementary school class; and five are made ill by this respiratory pathogen. Thus, 29 students continue to attend classes unaffected by influenza while five vulnerable ones are temporarily bedridden. The teacher might then wonder: “Do those five children represent a random sample of her class? Contrariwise, could any child in this small population of 34 have been attacked by influenza; or, alternatively, might some of her children, by biological nature or environmental circumstance, be more vulnerable than others to the ravages of this communicable disease?” And she might then reflect: “What, indeed, is the nature of vulnerability? Divinely determined or a reflection of very secular factors?”

Until such time in the distant future when effective vaccines to prevent all major communicable diseases will be available, an understanding of the epidemiological dynamics of communicable disease remains a vital part of public health policy. And so, the very existence of selective vulnerability—and its ramifications—remains a suitable subject of inquiry.

Let us assume a hypothetical population of 100 children all attending the same school class in some equally hypothetical city. Assume further that an airborne human virus has been introduced into the atmosphere of this classroom probably brought there by another child already incubating the disease. The vulnerability of these 100 children to a specific communicable disease may then be analyzed as a many-layered puzzle.

This airborne virus then takes root in some—but not all—of the children. Why? Immunologists will tell us that certain of these children, let’s guess at 13, were already immune to this specific virus strain either by having undergone a prior illness with it (thus rendering them immune) or by virtue of having been previously vaccinated against this specific strain of virus.

So now let us consider only those 83 remaining children with no prior “knowledge” of this virus. Of these, 77 will then develop clinical signs signifying that they have been duly infected. Again, a question. Somehow, six of those 83 children were allegedly exposed to the virus but were indifferent to it, did not come down with the disease. Exposure requires a physical intimacy with the virus but were indifferent to it, did not come down with the disease. Exposure requires a physical intimacy with the virus in question; and in the case of an airborne virus, physical proximity to the carrier expelling the virus into the ambient air.

Is it possible, in this hypothetical cluster of children, that some youngsters are more gregarious than others? That some, by virtue of their personalities, make more physical contact, more breathing in each others’ faces, than do others? And, contrariwise, may not some be more shy, more physically withdrawn? When poliomyelitis had been rampant, some seven decades ago, public health physicians noted that when children were, by circumstance, more isolated and participated less in group athletics, they were noticeably less vulnerable to clinical polio. And during the height of the polio epidemics, bedridden children, for whatever reason, did not develop paralytic disease. Two infectious diseases—influenza and polio—demonstrate a similar pattern of susceptibility: children less socially active (influenza) and children less physically active (polio) seem less vulnerable.

Verily, no two children are alike; but still these data show that the dynamics of human behavior may be instrumental in defining vulnerability to communicable disease.

Finally, let us consider those 77 children, of the original hypothetical group of 100, who went on to develop clinically apparent influenza. Would all 77 then demonstrate an equivalent degree of severity? Or, alternatively, might some have a more severe case of influenza than their sick classmates? Again, no two children are the same. In a recent retrospective study of Ohio children burdened by influenza, epidemiologists noted that those children with pre-existing diseases such as crooked spines (scoliosis) or asthma that might impair their capacity to breathe deeply were the children most severely affected by a respiratory disease such as influenza.

Life is not fair; nor is it a simple equation between good or evil, lucky or unlucky. In truth, our singular destinies are determined by countless secular variables. In centuries past, vulnerability or invulnerability to some infectious ailment, let us say bubonic plague, was hesitantly ascribed to ill-defined forces such as vindictive spells, one’s professed religion or divine fate. Today, we rely more on countless measurable factors—where and with whom we are, our inherited genomes, how we had conducted our lives and even random happenstance—to predict who amongst us develops a viral infection and who remains indifferent to its hazards.

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Disclosure of Financial Interests

The author and his spouse/significant other have no financial interests to disclose.

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**Sexually Transmitted Diseases: Introduction**

**Gail Skowron, MD**

**Sexually Transmitted Diseases (STDs),** also called Sexually Transmitted Infections (STIs), have been documented in the human population since at least the sixteenth century. The burden of disease from STDs has been closely tied to society's sexual practices, the availability of sensitive and specific diagnostic testing, and access to appropriate antibiotics. Recent advances in technology, such as smart phone sex-locator apps, and the rise of social media contribute to the spread of STDs today. Many STIs, including HIV, may be transmitted over the course of years, due to an infectious yet asymptomatic state.

In this issue, we address recent trends in STDs in Rhode Island and their optimal management. In general, STDs are most common in adolescents and young adults, who may be otherwise healthy and may not access medical care if asymptomatic. Primary care providers, as well as subspecialists, need to be comfortable taking a sexual history to identify risks for asymptomatic infection, vigilant for signs and symptoms that may indicate an STD, and able to initiate appropriate diagnostic testing and treatment or referral (Diaz, et al., *Sexually Transmitted Diseases in Primary Care*). The importance and the concomitant challenges of partner notification/contact tracing in the context of HIV and the 2010 rise in cases of infectious syphilis cases in Rhode Island is discussed by Alexander and colleagues from the Rhode Island Department of Health (*Interrupting Transmission of HIV and other Sexually Transmitted Infections in Rhode Island*). Infectious syphilis is further addressed with detailed diagnostic and management guidelines outlined by Skowron, et al. (*Infectious Syphilis: The Return of the Great Imitator to Rhode Island*). Kojic discusses the only vaccine-preventable STD, Human Papillomavirus (HPV), and the importance of more sensitive diagnostic tests and treatment of male partners in optimal management of *Trichomonas vaginalis* (Human Papillomavirus (HPV) and *Trichomonas: Common, Concerning, and Challenging Sexually Transmitted Infections*). *Chlamydia trachomatis* (the most common STD in Rhode Island) and *Neisseria gonorrhoeae* are associated with substantial long-term morbidity, including pelvic inflammatory disease, infertility, pregnancy complications and neonatal infections; Chan, et al., discuss improved diagnostic testing for these STDs in all exposed mucosal sites (*Recommendations for the Diagnosis of Neisseria gonorrhoeae and Chlamydia trachomatis, including Extra-genital sites.*). Post-exposure management of the above STDs, as well as HIV, Hepatitis B and Hepatitis C, is addressed by Hardy in a series of likely Q & As. (*Post-Exposure Testing and Treatment after Non-occupational Exposures To STDs and HIV*). Heightened awareness of STD trends in Rhode Island, their diagnosis and treatment, and how to facilitate partner notification and treatment, will move us closer to achieving the goal of reducing the incidence of STDs in the years to come.

Gail Skowron, MD, is Chief of the Division of Infectious Diseases at Roger Williams Medical Center and a Professor of Medicine at the Boston University School of Medicine.

**Disclosure of Financial Interests**

The author and/or their spouse/significant other have no financial interests to disclose.

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**Sexually Transmitted Diseases in Primary Care**

**Joseph A. Diaz, MD, MPH, Valeria Fabre, MD, and Marguerite A. Neill, MD**

**With approximately 19 million new sexually transmitted infections occurring each year, sexually transmitted diseases (STDs) are a major public health challenge** both nationally and in Rhode Island (Table 1). The clinical burden of STDs ranges from acute conditions to serious and even life-threatening sequelae including cancer, ectopic pregnancy, infertility, chronic pelvic pain, spontaneous abortion, stillbirth, low birth weight, prematurity, congenital and perinatal infections, neurological damage, and death. Women, minority populations, and adolescents are disproportionately affected by STDs. Although STDs affect people of all ages, races, and sexual orientation, nearly half of new STDs occur among young people (age 15–25 years), and the incidence of STDs and their sequelae are higher among African Americans and Latinos than among non-Latino Whites.

Most patients with STDs are treated by physicians in family or internal medicine, obstetrics or gynecology, making it critical that primary care providers (PCPs) are skilled and knowledgeable of components of STD management. Primary care physicians, however, often feel that their STD counseling skills are ineffective and their STD training inadequate. Many PCPs are unsure of STD treatment regimens and unfamiliar with CDC guidelines, presenting a barrier to appropriate screening as well as recognition and treatment of STDs. Many physicians are uncertain of STD reporting requirements and partner notification standards which likely contributes to the increasing disease burden locally and nationally.

Suppose a 24-year-old man with a new maculopapular rash or a 50-year-old woman who just learned her husband was having an affair came to your office as an acute visit. Do you know what questions to ask, what tests to order, whether to start treatment and with what, and what diagnoses to report to the Department of Health?
Taking a Sexual History

An effective sexual risk assessment starts with a thorough sexual history. Unfortunately, sexual health is under-addressed in US primary care settings. OF adults seen at a university primary care clinic 44% had never been asked their sexual history. Another survey reported that while 58% of primary care doctors asked patients about sexual activity, only a few asked for additional details. Factors contributing to this gap are clinician discomfort and lack of interview skills for the topic, and patients’ disquiet in discussing sexual practices with their doctors and fear of disapproval.

A sexual history should be taken in a professional, sensitive and non-judgmental manner, and patients reassured of confidentiality. The question “Are you sexually active? ” can be followed by “do you have sex with men, women or both?” creating an atmosphere of open communication. The CDC proposes the “5Ps” as an effective way to elicit the most relevant information of the sexual history (Table 2). The “5 Ps” refers to:

1. Partners
   “Do you have sex with men, women or both?”
   “In the past 2 months, how many partners have you had sex with?”
   “In the past 12 months, how many partners have you had sex with?”
   “Is it possible that any of your sex partners in the past 12 months had sex with someone else while they were still in a sexual relationship with you?”

2. Prevention of pregnancy
   “What are you doing to prevent pregnancy?”

3. Protection from STDs
   “What do you do to protect yourself from STDs and HIV?”

4. Practices
   “To understand your risks for STDs, I need to understand the kind of sex you have had recently.”
   “Have you had vaginal sex, meaning ‘penis in vagina sex’?”
   If yes, “Do you use condoms: never, sometimes, or always?”
   “Have you had anal sex, meaning ‘penis in rectum/anus sex’?”
   If yes, “Do you use condoms: never, sometimes, or always?”
   “Have you had oral sex, meaning ‘mouth on penis/vagina’?”
   For condom answers:
   If “never”: “Why don’t you use condoms?”
   If “sometimes”: “In what situations (or with whom) do you not use condoms?”

5. Past history of STDs
   “Have you ever had an STD?”
   “Have any of your partners had an STD?”
   Additional questions to identify HIV and viral hepatitis risk include:
   “Have you or any of your partners ever injected drugs?”
   “Have any of your partners exchanged money or drugs for sex?”
   “Is there anything else about your sexual practices that I need to know about?”

Table 1. Trends in STDs, US and RI, 2010

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>US Cases</th>
<th>RI Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia trachomatis</td>
<td>1,307,893</td>
<td>3,480</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>309,341</td>
<td>291</td>
</tr>
<tr>
<td>Syphilis (primary and secondary)</td>
<td>13,774</td>
<td>61</td>
</tr>
<tr>
<td>Herpes simplex</td>
<td>Estimated 1 million</td>
<td>(not reportable)</td>
</tr>
<tr>
<td>HIV</td>
<td>40,000 new cases</td>
<td>106</td>
</tr>
<tr>
<td>HPV</td>
<td>Estimated 5.5 million</td>
<td>(not reportable)</td>
</tr>
</tbody>
</table>

STD Clinical Syndromes

Early diagnosis and treatment are key to easing the clinical and public health burden of STDs. For the primary care doctor genital lesions are easily recognized as a possible STD. However, patients may present with non-genital manifestations and therefore pose a diagnostic challenge.

Clinical symptoms and findings affecting the genital area may be grouped into syndromes associated with specific organisms (Table 2). The prevalence and incidence of STDs vary depending on the region and population analyzed. A recent observational study of STDs and HIV infected patients in the primary care setting reported that the most commonly diagnosed infections were rectal chlamydia, oropharyngeal gonorrhea, and chlamydial urethritis among the men and trichomoniasis among the women.
Each STD genital syndrome is not pathognomonic for a single specific pathogen. There are also geographic considerations for some agents such as chancroid, common in tropical areas but uncommon in the US. These considerations provide the rationale for testing for more than one pathogen at the time of presentation and for followup assessment of response to treatment.

The non-genital manifestations of STDs refer to a wide range of physical findings outside the genital tract (Table 4). Some are seen commonly in primary care (pharyngitis, skin rash) and clinicians unaware of the association with an STD will miss the opportunities to obtain relevant history and subsequently, appropriate testing. Some clinical presentations are rapidly linked to a specific STD like Pneumocystis pneumonia and HIV. Others are well known associations but easier to miss because they are less common, such as recurrent aseptic meningitis (Mollaret meningitis) and HSV-2 (12). Lastly, clinicians should also be aware that some pathogens do not cause STDs but can be transmitted sexually, such as the viral hepatitides A, B and C, *Giardia lamblia*, *Entamoeba histolytica* and *E. dispers*.

### DIAGNOSTIC TESTING

Clinicians will usually need to first consider the clinical context for STD testing so that the correct tests are performed. Patient age and sex, whether asymptomatic, presence (and history) of clinical signs or symptoms and number of sex partners will be important parameters for initial assessment. Use of condoms and/or microbicides can decrease risk of STD transmission but not to the point of obviating testing.

Testing for STDs can be confusing, in part because of the need to usually test for pathogens simultaneously, the different types of tests and the specifics of which clinical specimen is appropriate. The most common of the currently available tests used in the US are summarized in Table 5.

Most circumstances surrounding STD evaluation entail simultaneous testing for more than one pathogen for several reasons: first, transmission can occur from asymptomatic individuals infected with more than one pathogen; second, some patients have multiple sex partners; third, genital ulcer disease increases the risk for transmission of other non-ulcerative STDS. The pathogens for which simultaneous testing is most commonly done in the US include *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, syphilis and HIV, all of which can have long asymptomatic periods during which patients are infectious to others. Because transmission of these pathogens to partners or offspring is a potential high impact occurrence, routine inclusion of screening for these in several settings is emphasized rather than screening based on perceived risk.

The two patients mentioned in the Introduction should be tested for chlamydia, gonorrhea, syphilis and HIV, with HSV PCR of any genital or rectal ulcers if present.

### NEWER HIV TESTING REGULATIONS IN RHODE ISLAND

To foster earlier diagnosis and limit transmission, changes have been made to HIV testing in RI that went into effect over 2008 – 2010. HIV testing is to be offered in all health care settings as part of routine medical care including prenatal care. Verbal consent for testing is now acceptable but must be documented in the chart. There also should be documentation on the information about HIV testing that was provided to the patient. Discussion of the results should include counseling tailored to the individual patient’s circumstance. Annual screening (or more frequently) should be offered to those at high risk, such as those with multiple sexual partners. Neonates without documented prenatal testing can be tested at birth.  

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Symptoms</th>
<th>Signs</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal discharge</td>
<td>Vaginal discharge Dysuria Dyspareunia</td>
<td>Abnormal vaginal discharge</td>
<td>Vaginitis: -Trichomonas Cervicitis: -Gonorrhea -Chlamydia</td>
</tr>
<tr>
<td>Urethral discharge Dysuria</td>
<td>Urethral discharge Urinary frequency</td>
<td>Urethral discharge</td>
<td>Gonorrhea Chlamydia</td>
</tr>
<tr>
<td>Genital ulcer</td>
<td>Painless Painful Painful Painless</td>
<td>Indurated base Necrotic material</td>
<td>Syphilis Chancroid Genital herpes LGV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Beefy red, rolled edges</td>
<td>Granuloma inguinale</td>
</tr>
<tr>
<td>Genital wart</td>
<td>Genital wart</td>
<td>Genital wart</td>
<td>Syphilis HPV</td>
</tr>
<tr>
<td>Lower abdominal pain</td>
<td>Dyspareunia Lower abdominal pain</td>
<td>Vaginal discharge Abdominal tenderness on exam Temp &gt;38°C</td>
<td>Gonorrhea Chlamydia</td>
</tr>
<tr>
<td>Scrotal swelling and pain</td>
<td>Scrotal swelling</td>
<td>Scrotal swelling</td>
<td>Gonorrhea Chlamydia</td>
</tr>
<tr>
<td>Inguinal lymphadenopathy</td>
<td>Painful enlarged inguinal lymph nodes</td>
<td>Enlarged inguinal lymph nodes Abscess or fistula</td>
<td>LGV Chancroid</td>
</tr>
</tbody>
</table>

Adapted from Training modules for the syndromic management of sexually transmitted infections 2007, accessed from http://www.who.int/topics/sexually_transmitted_infections.
Table 4. Non-genital manifestations of STDs.

<table>
<thead>
<tr>
<th>Clinical finding</th>
<th>Possible Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constitutional symptoms (fever, malaise, weight loss, sore throat)</td>
<td>Secondary syphilis, acute HIV, acute HBV</td>
</tr>
<tr>
<td>Ocular</td>
<td>Syphilis, Gonorrhea</td>
</tr>
<tr>
<td>uveitis, optic neuritis</td>
<td></td>
</tr>
<tr>
<td>purulent conjunctivitis</td>
<td>Chlamydia</td>
</tr>
<tr>
<td>inclusion conjunctivitis</td>
<td></td>
</tr>
<tr>
<td>Oral ulcers and mucosal patches</td>
<td>Syphilis, HIV</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>Syphilis, acute HIV, gonorrhea</td>
</tr>
<tr>
<td>Generalized lymphadenopathy</td>
<td>Syphilis, HIV</td>
</tr>
<tr>
<td>Skin rash</td>
<td>Secondary syphilis, HIV, gonorrhea</td>
</tr>
<tr>
<td>maculopapular</td>
<td></td>
</tr>
<tr>
<td>pustular</td>
<td></td>
</tr>
<tr>
<td>seborrheic dermatitis</td>
<td></td>
</tr>
<tr>
<td>Herpes zoster</td>
<td></td>
</tr>
<tr>
<td>Molluscum contagiosum</td>
<td></td>
</tr>
<tr>
<td>vasculitis</td>
<td></td>
</tr>
<tr>
<td>photosensitivity and blistering</td>
<td></td>
</tr>
<tr>
<td>(sporadic porphyria cutanea tarda)</td>
<td></td>
</tr>
<tr>
<td>lichen planus</td>
<td></td>
</tr>
<tr>
<td>Alopecia</td>
<td>Syphilis</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Gonorrhea, HBV</td>
</tr>
<tr>
<td>Aseptic meningitis</td>
<td>HSV, Syphilis, HIV</td>
</tr>
<tr>
<td>Respiratory</td>
<td>HIV</td>
</tr>
<tr>
<td>Pneumocystis pneumonia</td>
<td></td>
</tr>
<tr>
<td>Severe bacterial pneumonia</td>
<td></td>
</tr>
<tr>
<td>GI</td>
<td>HIV</td>
</tr>
<tr>
<td>Oral or esophageal candidiasis</td>
<td>HIV</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>HBV, HCV, HIV, Syphilis</td>
</tr>
<tr>
<td>Perihepatitis</td>
<td>Chlamydia and gonorrhea</td>
</tr>
<tr>
<td>Chronic diarrhea</td>
<td>HIV</td>
</tr>
<tr>
<td>Proctitis and ulcerative colitis-type picture</td>
<td>LGV</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>HCV, HBV, syphilis</td>
</tr>
</tbody>
</table>

Table 5. Common Tests for STD Diagnosis

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Testing</th>
<th>Specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. trachomatis</td>
<td>Nucleic acid amplification tests (NAATs)</td>
<td>Urine (20-30 ml) of first catch without cleaning genitalia; use container without preservatives; transport to lab ASAP; process &lt; 24hrs from collection Cervical, self-collected vaginal, male urethral or rectal swab with special swab from test kit</td>
</tr>
<tr>
<td></td>
<td>Not all NAATs are FDA cleared for all clinical specimens</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Syphilis, HIV</td>
<td>Serum or plasma; CSF VDRL</td>
</tr>
<tr>
<td></td>
<td>Gonorrhea</td>
<td>Culture (special media)</td>
</tr>
<tr>
<td></td>
<td>Syphilis</td>
<td>Usually 2-step Ab testing; Initial non-treponemal test (VDRL or RPR); if positive, confirmation with treponemal test (FTA-ABS) and VDRL or RPR titer</td>
</tr>
<tr>
<td></td>
<td>Herpes simplex</td>
<td>PCR preferred over culture; Swab of genital or rectal ulcer using swab from special collection kit</td>
</tr>
<tr>
<td></td>
<td>HIV</td>
<td>HSV type specific IgG in some situations</td>
</tr>
<tr>
<td></td>
<td>HPV</td>
<td>Clinical appearance of genital warts and response to treatment Cervical cancer screening in women &gt; 30yrs</td>
</tr>
<tr>
<td></td>
<td>HIV</td>
<td>Serum or plasma</td>
</tr>
<tr>
<td></td>
<td>Quantitative viral load</td>
<td>Blood</td>
</tr>
<tr>
<td></td>
<td>HPV</td>
<td>Biopsy in selected cases Viral nucleic acid or capsid protein detection</td>
</tr>
</tbody>
</table>
STD TREATMENT AND REPORTING

STDs are reportable in RI and embedded in the report is requested documentation of treatment. Current treatment regimens for STDs (including drug, dose and duration) are found on the RI confidential case report form.14

PARTNER MANAGEMENT

Of substantial importance in STD treatment and control is partner management.8 This starts with partner notification with follow through for their evaluation and treatment. Clinicians can encourage and support the index patient with partner notification, or if the patient is unwilling or unable, specific assistance can be requested from the RI DOH. Expedited partner therapy (EPT) is permissible by RI regulation for sex partners of persons with chlamydia or gonorrhea, allowing the provision of a prescription or pills for the sex partner without prior evaluation. However, EPT is not recommended for men who have sex with men.14

PREVENTION

Primary prevention of STDs starts with education on risk reduction and avoidance. Vaccination, preferably pre-exposure, can prevent sexual transmission of HAV, HBV, and HPV. Secondary prevention includes rapid diagnosis and treatment along with partner management of persons with overt clinical disease as well as those asymptomatically infected.

RESOURCES

Information on Rhode Island case reporting, partner services and specialty referral:

http://www.health.ri.gov/diseases/sexuallytransmitted/for/providers/

Expedited Partner Therapy for STDs: Guidance for Medical Providers in Rhode Island:


CDC Training Courses and STD Educational Materials:

http://www.cdc.gov/std/training/default.htm

REFERENCES


Disclosure of Financial Interests

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Medicine & Health/Rhode Island
Interrupting Transmission of HIV and Other Sexually Transmitted Infections in Rhode Island

Nicole E. Alexander, MD, MPH, Philip A. Chan, MD, Tanya O. Rogo, MD, MPH, Zoanne Parillo, Carol A. Browning, MS, RN, BC, Brittany S. Isabell, MPH, Casandra Calcione, Sutopa Chowdhury, MBBS, MPH, Peter Simon, MD, MPH, and Rami Kantor, MD

In this paper we highlight the epidemiology of HIV and other STI transmission in RI and the methods in place to interrupt it.

Epidemiology of HIV and Other STI

Current epidemiology of HIV and other STIs in RI is concerning and reflects the national epidemic, with ongoing and increasing transmissions throughout the state, particularly among MSM. Demographic characteristics for individuals with chlamydia, gonorrhea, HIV, and syphilis, all reported to HEALTH, reveal highest proportions in Providence County (81-91% of STIs and 77% of HIV) in 2010.1 Comparison of infection rates between 2009 and 2010 demonstrate stable chlamydia (344 vs. 331 cases per 100,000 population; 3615 vs. 3480 total cases); gonorrhea (31 vs. 28 cases per 100,000; 322 vs. 291 total cases); and HIV infections (12 vs. 10 per 100,000; 125 vs. 106 total cases); but increased infectious syphilis infections (3 vs. 6 cases per 100,000; 34 vs. 61 total cases of primary, secondary, and early latent syphilis); a 79% increase.1 (Table 1)

Traditional Epidemiological Methods of Interrupting Disease Transmission – Partner Notification

To control HIV and other STI transmission, in addition to collecting demographic characteristics, HEALTH identifies potential sexual partners of index cases and notifies these partners of their potential exposure to gonorrhea, syphilis, and HIV (i.e. contact tracing or partner notification). Sexual partners of chlamydia cases are not notified due to the high case volume, except with prioritized cases or upon provider request.

Five methods of partner notification are employed with varying levels of effectiveness. (1) Provider referral: a specifically-trained health department employee, often referred to as a partner notification specialist or disease intervention specialist (PNS/DIS), interviews the index case, obtains their possible sexual partners and notifies them; (2) Third party referral: professionals other than HEALTH staff members carry out partner notification (e.g., HIV counselors or clinicians); (3) Self-referral: index cases choose to notify their sexual partners on their own; (4) Contract referral: the index case agrees to notify partners and if not successful or completed, the provider then intervenes and follows-up; and (5) Dual referral: both the index case and the provider notify partners of potential sexual exposures. Provider referral has been shown to be the most effective single method for partner notification, while self-referral is the least effective.3 Given that more partners are treated through partner notification services rather than through other strategies, treatment of sexual partners is valuable for control of infection and cost-effective for averting

Table 1. Sexually transmitted infection rates and total cases in Rhode Island, 2009 – 2010

<table>
<thead>
<tr>
<th>Rate of infection</th>
<th>2009</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia cases per 100,000 population (total cases)</td>
<td>344 (3615)</td>
<td>331 (3480)</td>
</tr>
<tr>
<td>Gonorrhea cases per 100,000 population (total cases)</td>
<td>31 (322)</td>
<td>28 (291)</td>
</tr>
<tr>
<td>HIV cases per 100,000 population (total cases)</td>
<td>12 (125)</td>
<td>10 (106)</td>
</tr>
<tr>
<td>Syphilis cases per 100,000 population (total cases)</td>
<td>3 (34)</td>
<td>6 (61)</td>
</tr>
</tbody>
</table>
sequelae of disease. HEALTH utilizes any of the partner notification methods that a provider or patient prefers, with provider referral being the most common.

Effectiveness of partner notification is dependent on a close collaboration between health department PNS/DIS personnel and community health care providers. The first essential step in the control of disease transmission is the reporting of a syphilis, gonorrhea, or HIV case to HEALTH. This reporting can be done using the case report forms available on the HEALTH website (www.health.ri.gov → ‘Information for Healthcare Providers’ → ‘Report certain diseases and conditions to the department’ → ‘HIV/AIDS (Adult Confidential)’ and ‘Sexually Transmitted Diseases’). Given the important nature of timely intervention, as soon as the partner notification services team is aware of a new index case, the PNS/DIS attempts to contact this individual for counseling and interviewing. During that process, a list of sexual partners is elicited from the individual, including contact information that the index case is able to provide such as telephone numbers, email addresses, and/or social media information. The partners contacted are offered risk reduction counseling, rapid HIV testing, referral for other STI testing, and linkage to medical care. An index case’s name, gender, and the time period of potential sexual exposure are not revealed to the notified partners. The process of identifying and reaching sexual partners of index cases can be substantially enhanced when it is encouraged and facilitated by the provider involved. Providers can make patients aware that HEALTH personnel will be contacting them to initiate the partner notification service. Effective communication between PNS/DIS and health care providers is essential and can lead to successful interruption of transmission in the chain of HIV and other STIs.

**Implementation of Partner Notification Services for Syphilis Exposure**

The number of new infectious syphilis cases reported to HEALTH in 2010 was 61 (58 males; 3 females). PNS/DIS attempted to interview 100% of those cases, and was able to successfully interview 58/61 (95%) of them; documented reasons for the remaining three not interviewed were refusal (1) and unknown reasons (2). From the 58 index cases, 133 partners were elicited through the partner notification process. (Figure 1) Thirty of these 133 partners (23%) were examined by a provider upon referral from HEALTH, resulting in preventative treatment in 12/30 (40%) and treatment of confirmed syphilis infection in 5/30 (17%). The remaining 13/30 (43%) referred to care did not have preventative treatment, according to clinical judgment, and patient preference. Of the 103/133 partners that were not examined by a health care provider, 16/133 (12%) reported previous appropriate treatment, and 87/133 (65%) were not evaluated by a provider for a variety of reasons, including refusal (11/87, 13%), inability to locate despite having sufficient information (14/87, 16%), or insufficient contact information (61/87, 70%). Anonymous sexual activity among infectious syphilis cases was reported by 33% (1/3) of females; 25% (1/4) of heterosexual males; and 61% (33/54) of MSM with infectious syphilis in 2010.
Implementation of Partner Notification Services for HIV Exposure

One hundred and six new HIV cases were reported to HEALTH in 2010, and 100% were sought after for interview by HEALTH’s PNS/DIS. Of the 106 cases, 93% (99/106) were successfully reached. There were three reasons seven index cases were not reached for an interview: (1) they were noted to be previously HIV positive and already interviewed as a new case, (2) they were not able to be reached based on insufficient or inaccurate information, or (3) they refused to communicate. Among the 99/106 index cases reached, 94/99 (95%) were willing to accept partner notification services with behavior risk reduction counseling, an interview, and referral to care. Ranging from one reported partner per index case to 500 partners per index case, 942 total partners were elicited from these 94 new HIV index cases through the partner notification process. A major proportion of these partners were unable to be identified by HEALTH’s PNS/DIS because of anonymous sexual activity; a smaller proportion of partners were unable to be located because the index case refused to name the partners and did not want the PNS/DIS to contact the exposed partners; or because partners resided out-of-country. PNS/DIS submitted information about out-of-state partners to other state health departments for notification. Among 71 sexual partners with locatable contact information, 66 (93%) were reached and notified of their exposure to HIV and other potential STIs. HIV testing was performed on 56/66 (85%), including rapid HIV testing at the time of notification. The remaining 10/66 (15%) were not tested for HIV due to declined testing (2/10), a known positive HIV status (4/10), or a prior HIV negative test within the last one to three months, depending on the last unprotected sexual exposure (4/10).

Nine percent (5/56) of HIV-tested sexual partners of index cases were newly identified and confirmed as HIV positive in this partner notification process. Two of the five newly diagnosed cases self-identified as MSM, one self-identified as transgender (male to female), and two were heterosexual females.

Novel Exploratory Methods of Interrupting Disease Transmission – Molecular Epidemiology

The high number of anonymous partners reported among HIV index cases highlights the challenges of partner notification as a means of HIV and other STI transmission prevention. Technological advances have enabled people to easily meet anonymous partners through venues such as internet social networks and chat rooms, as well as through smartphones and other mobile devices. A survey of middle and high school students in several Northeastern states found that 35% of high school boys and 37% of high school girls reported meeting a stranger on-line, and 23% of boys and 13% of girls reported that some sort of sexual encounter occurred at the ensuing face-to-face meeting. Technology has given rise to new social norms and mechanisms that people can use to find sex partners, thus creating novel ways in which sexual networks form and influence the transmission and incidence of HIV and other STIs. Incorporation of molecular epidemiology in HIV prevention is a novel approach to further assist the traditional partner notification services at interrupting the transmission of HIV and other STIs.

In the context of HIV, molecular epidemiology involves the use of phylogenetics and statistics to reconstruct and examine the evolutionary patterns of genetic sequences on the virus, looking for closely related sequences. These tools, unless used for forensic investigations involving more complex methods, cannot and do not intend to infer direct transmission between individuals who harbor closely related sequences, and it is impossible to determine direct transmission between them, whether other individuals are involved, or whether they are completely unrelated. However, molecular epidemiology can describe patterns of HIV transmission in a population, and this approach has been used to study HIV outbreak investigations, and trends and dynamics of HIV in different populations, including in RI.

While molecular epidemiology has the ability to improve our knowledge of HIV transmission patterns by identifying specific transmission networks at a molecular resolution, the HIV and other STI partner notification programs at HEALTH will continue to benefit from collaboration with health care providers to facilitate communication with infected patients, identification of partners, and promotion of testing and linkage to care. The effectiveness of combining these traditional and novel methods needs to be explored, a process that is ongoing in RI.

Conclusion and Challenges to Overcome

Interrupting HIV and other STI transmission in RI is an essential goal that requires state-wide involvement at all levels of health care, community service organizations, and public health officials. Testing for these infections should be routine for all individuals engaged in sexual activity, regardless of sexuality. Once such testing practices are in place to better identify new cases, steps can be taken to improve this process further. Some common challenges in the partner notification process for HEALTH are the delay in receiving timely and complete case report forms with sufficient demographic information. This results in (1) numerous attempts by HEALTH to communicate with the provider for the necessary information, and (2) a delay in the opportunity to effectively initiate the partner notification services. Licensed health care providers and facilities are asked to report HIV and other STIs within four days of diagnosis, to help identify additional infected cases and their sexual partners earlier in the disease transmission process.

High numbers of anonymous sexual partners of index cases present significant challenges to partner notification, and to the interruption of further transmitting infections. Anonymous sexual partners do not usually exchange demographic information, making the process of locating exposed partners extremely difficult. Although anonymous sexual activity may take place at venues such as bath houses or other sex club venues, an increasing proportion of sexual contacts occur through social media such as internet sites or anonymous sex smartphone applications. HEALTH PNS/DIS personnel currently work with these social media tools to improve partner notification. Integration of molecular epidemiology with partner notification programs to further address...
this challenge may allow improved risk reduction counseling with better understanding about sexual behavior patterns and targeted prevention interventions.

Health care providers are essential facets in enhancing the goal to reduce transmission of HIV and other STIs in RI, by being aware of the opportunities to interrupt further spread of disease and working with HEALTH to facilitate these efforts. In addition to routine testing and quick reporting of new cases, providers can perform or encourage partner notification by educating patients about the process and the potential for communication by PNS/DIS staff from HEALTH. Partner notification services can also be requested from HEALTH by health care providers to help locate or counsel patients who do not return to be informed of their new HIV and other STI positive results. A strong collaboration across agencies, particularly between health care providers and HEALTH will be crucial to effectively interrupt further transmission of HIV and other STIs in RI.

REFERENCES


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Infectious Syphilis: The Return of the Great Imitator To Rhode Island
Gail Skowron, MD, Xiaodan Wang, MD, and Ekta Gupta, MD

Since 2010, Rhode Island has seen a precipitous increase in the number of cases of infectious syphilis, particularly among HIV+ men who have sex with men (MSM). As clinicians, we are charged with recognizing the protean manifestations of this ancient disease, often called “the Great Imitator,” a task made difficult by the low prevalence of syphilis during our training and practice. Entire textbooks have been devoted to the topic of syphilis; this article is designed as a clinical primer on infectious syphilis for the practicing clinician in primary care, emergency medicine, dermatology, neurology, hepatology, and nephrology. In order to contribute to public health efforts to reduce the spread of syphilis (see accompanying article “Interrupting Transmission of HIV and Other Sexually Transmitted Infections in Rhode Island”), emphasis is placed on the diagnosis of infectious syphilis (primary, secondary and early latent) in adults.

Etiology
Syphilis is caused by Treponema pallidum, a slender, tightly coiled bacterium that cannot be cultivated in vitro. The genome of T. pallidum lacks apparent transposable elements, suggesting that the genome is extremely conserved and stable. This is the likely explanation of why T. pallidum has remained exclusively sensitive to penicillin for more than 70 years and that there are few differences in DNA sequences among subspecies.

History & Epidemiology
Syphilis has a long and storied past. Historians have speculated that Columbus brought syphilis back to Europe from the New World, perhaps leading to the “Great Pox” epidemic in Europe and Asia. In the United States, syphilis cases reached a peak during World War II, and declined steadily with the use of serologic testing and penicillin therapy until the late 1980s and early 1990s, when an increase in cases in heterosexual women and neonates was linked to exchange of sex for drugs, particularly crack cocaine. After declining once again by 2000, a more recent rise in cases has been noted in men who have sex with men. In Rhode Island, the number of infectious syphilis cases per year rose from 25 in 2008 to 61 in 2010. In 2010, 93% of cases were in MSM and half of those were HIV-infected. Factors associated with syphilis infection included engagement in anonymous sex and finding sexual partners online. This epidemiology necessitates all physicians to complete a comprehensive assessment of sexual practices, and testing for HIV infection and other sexually transmitted diseases.

Syphilis can be acquired by sexual contact, transplacental transfer, kissing or other close contact with an active lesion, transfusion of contaminated fresh human blood, or accidental direct inoculation (needlestick).

Clinical Manifestations
Primary Syphilis
The classic syphilitic chancre occurs at the site of inoculation of the spirochete, and may be seen as single or multiple genital, perianal, or oral lesions. The chancre is characteristically indurated with a rolled edge and clean base, painless, and accompanied by regional lymphadenopathy. Lesions may be inapparent to the patient. The median incubation period before appearance of the chancre is 21 days, with a range from three to 90 days after acquisition. Syphilitic chances are not reliably diagnosed by any serologic test and, given the lack of ready availability of dark-field microscopy, these must be diagnosed clinically and managed presumptively (treatment, reporting, follow-up and partner management).

Secondary Syphilis
The clinical presentation of secondary syphilis is protean, as one would expect from the wide dissemination of treponemes throughout the body during the spirochtemia of early infection. The presentation most easily remembered from medical school is a rash with the classic “palms and soles” distribution. (Figure 1)

Table 1. Multi-organ system manifestations of Secondary Syphilis (modified from Mandell PPID)

| Skin                    | Generalized rash | begins on the trunk, typically non-pruritic |
|                        |                  | macules then papules, may be scaly, rarely pustular |
|                        |                  | classically involves palms & soles |
| Condylomata lata       | highly infectious |
|                        | painless, broad, moist, gray-white to erythematous plaques |
|                        | occur in warm, moist areas |
| Mucous patches         | highly infectious |
|                        | silvery gray, superficial erosion with a red periphery |
|                        | occur on oral, genital, anal mucous membranes |
| Constitutional symptoms | low-grade fever, malaise, pharyngitis, laryngitis, anorexia, weight loss, arthralgias |
| Lymphadenopathy        | generalized painless lymphadenopathy |
|                        | enlargement of the epitrochlear lymph nodes is a unique finding that should always suggest the diagnosis of syphilis |
| Neurologic             | CNS involvement in up to 40% of patients |
|                        | Headache and meningismus are common |
| Ocular syphilis        | Anterior or posterior uveitis or panuveitis, episcleritis, vitreitis, retinitis, papillitis, interstitial keratitis, acute retinal necrosis, and retinal detachment |
|                        | differential diagnosis includes tuberculosis, rheumatoid arthritis, sarcoidosis, toxoplasmosis, histoplasmosis, and ocular Toxocara canis infections |
| Otic syphilis          | sudden or progressive sensorineural hearing loss, tinnitus, vertigo, and dysequilibrium |
| Hepatic                | high serum alkaline phosphatase level, a normal or moderately elevated serum bilirubin concentration |
| Kidney                 | immune complex glomerulonephritis, with subepithelial electron-dense deposits |
Patients may ascribe the rash to another etiology, and, though classically non-pruritic, they may present with the common “generalized pruritic rash” to their primary care provider. (Figure 2) The lesions typically begin as three to ten mm macules, symmetrically distributed first on the trunk and upper extremities, that may progress to papules, and less commonly, to pustules. A fine scaly appearance is seen in papulosquamous rashes. The lesions on the palms and soles are typically reddish brown, flat or with a scaly appearance. A patchy alopecia or loss of eyebrows and beard may occur.1,7 These skin lesions are not infectious to intact skin, though the use of gloves is recommended when examining any potentially infectious rash. Vesicular lesions occur only in congenital syphilis.1

Two highly infectious skin lesions are condylomata lata and mucous patches. Condylomata lata occur on warm, moist, intertriginous areas (perianal area, vulva, scrotum, inner aspects of the thighs, skin under pendulous breasts, nasolabial folds, cleft of the chin, axillary and antecubital folds, webs of the fingers and toes) as painless, broad, moist, grey-white to erythematous plaques.1 Mucous membrane lesions, termed mucous patches, are silvery gray, superficial erosion with a red periphery, and may occur on lips, mouth, pharynx, tonsils, vulva, vagina, glans penis, inner prepuce, cervix, and anal canal.1

Constitutional symptoms may be prominent (or the presenting complaint), including fever, malaise, pharyngitis, anorexia, weight loss, and arthralgias. Generalized lymphadenopathy (particularly epitrochlear), hepatitis, and glomerulonephritis may accompany other manifestations. Seeding of the central nervous system may occur at any stage of syphilis, and early neurologic disease (syphilitic aseptic meningitis, ocular and otic syphilis) may occur.1 Acute HIV infection is in the differential diagnosis of secondary syphilis, both due to overlapping clinical presentation and shared modes of transmission, and all patients diagnosed with syphilis should have HIV testing performed.

Early Latent Syphilis

Latent syphilis is by definition seroreactivity without other evidence of disease. Early Latent syphilis is defined as 1) documented seroconversion or fourfold rise in titer in the past year, or 2) unequivocal symptoms of primary or secondary syphilis (now resolved), or 3) a sex partner documented to have primary, secondary, or early latent syphilis.6 Late Latent syphilis is defined as asymptomatic seroreactivity in the absence of these conditions. Early latent syphilis is considered “early” or “infectious” syphilis and treatment recommendations are identical to primary and secondary syphilis.

To LP or not to LP?

A common clinical dilemma is whether to perform an LP on a patient presenting with early syphilis.8 This is particularly true for HIV-infected patients, in whom an increased likelihood of progression to symptomatic neurosyphilis has been described.9 In HIV+ individuals, clinical and CSF abnormalities consistent with neurosyphilis are associated with an RPR titer > 1:32 and/or a CD4 cell count < 350 cells/µL.11-13 However, no studies have demonstrated a change in clinical outcome if a lumbar puncture is performed and neurosyphilis is documented and treated.8,14 Therefore, CDC does not recommend CSF examination in HIV-infected or -uninfected patients who lack neurologic signs or symptoms suggestive of neurosyphilis.7 In clinical practice, therefore, a detailed history and physical examination to detect symptomatic neurosyphilis must be performed in all patients diagnosed with syphilis. If clinical evidence of neurologic involvement is observed (e.g., cognitive dysfunction, motor or sensory deficits, ophthalmic or auditory symptoms, cranial nerve palsies, and symptoms or signs of meningitis), an evaluation that includes CSF analysis, ocular slit-lamp ophthalmologic examination, and otologic examination should be performed. Treatment should be guided by the results of this evaluation.6

Laboratory Diagnosis

The serologic diagnosis of syphilis relies on the use of non-treponemal (RPR, VDRL) and treponemal tests (FTA-ABS, EIA). In Rhode Island, an RPR/VDRL screening test can be performed rapidly in the clinical laboratory. All samples testing positive by the non-treponemal RPR/VDRL assay are confirmed by the treponemal FTA-ABS test. The RPR/VDRL tests are subject to a false-negative “prozone effect,” due to high antibody titers, particularly in secondary syphilis. In cases where syphilis is highly suspected, the lab should be asked to repeat
the test using higher dilutions of serum. False positive RPR/VDRL tests may occur in collagen vascular disease, pregnancy, intravenous drug use, advanced malignancy, tuberculosis, malaria, viral and rickettsial diseases, and advanced age. A false positive FTA may result from cross-reactivity with other spirochetes, such as *Borrelia burgdorferi*, the etiologic agent of Lyme Disease.1

New rapid treponemal tests, such as the Syphilis EIA or chemiluminescence immunoassay, have been utilized to accomplish low-cost, automated, high-volume syphilis screening. If the rapid treponemal test is positive, an RPR/VDRL with titer must be performed to distinguish active from past infection.15

The laboratory diagnosis of neurosyphilis is made difficult by the lack of a standard definition.9 A positive CSF VDRL in the absence of substantial contamination of CSF with blood, is considered diagnostic of neurosyphilis.16 However, this test is relatively insensitive, thus a negative CSF VDRL does not rule out neurosyphilis (i.e., helpful only if positive). Other diagnostic criteria include CSF pleocytosis (> 5 cells/mm³ in HIV uninfected, >10-20 cells/mm³ in HIV-infected) and elevated CSF protein.17,18 In HIV patients who are not on antiretroviral therapy, these abnormalities are common, making it difficult to ascribe CSF abnormalities to neurosyphilis in the absence of a positive CSF VDRL.18,19 The CSF FTA-ABS is highly sensitive but not specific, thus, if negative, neurosyphilis is highly unlikely (i.e., helpful only if negative).6,14,19

**LABORATORY TESTING FOR OTHER STDs**

Syphilis, HIV, gonorrhea and chlamydia are transmitted person-to-person by similar sexual practices.20,21 Individuals testing positive for syphilis, therefore, should be screened for other STDs. Testing should target areas of exposure, i.e., urine gonorrhea and chlamydia (all patients), rectal gonorrhea and chlamydia (anal receptive patients), pharyngeal gonorrhea (oral receptive patients), vaginal trichomonas and bacterial vaginosis/cervical gonorrhea and chlamydia (vaginal receptive women). Patients may state they “always practice safe sex” but on specific questioning, may admit to unprotected oral sex; while this is less risky for transmission of HIV infection, the localization of syphilis organisms on external genitalia during primary and secondary syphilis provides ample opportunity for transmission during oral sex. This underscores the need to look for the lesions of primary syphilis in and around the mouth. Patients testing negative for HIV on this initial evaluation should be considered for re-testing in three months.

**TREATMENT OF EARLY (INFECTIOUS) SYphilIS**

Early or Infectious syphilis includes primary syphilis, secondary syphilis and early latent syphilis, all of which are treated with the same regimen of one injection of Benzathine Penicillin G 2.4 MU intramuscularly. (Table 2) The CDC and RI Department of Health strongly recommend that clinicians always use Benzathine Penicillin whenever possible. In practice, this may require some investigation into the details of reported penicillin allergy and mandates penicillin desensitization for pregnant women and patients diagnosed with neurosyphilis. Alternative regimens for treatment of early syphilis in patients with a history of severe penicillin allergy are: Doxycycline 100 mg po BID x 14 days; Ceftriaxone 1 g IM or IV QD x 10-14 days; Azithromycin 2 g po x 1. All of these regimens have reduced efficacy, increasing resistance and/or a paucity of supporting clinical data, and should only be used when patients are unable to be treated with penicillin. HIV-negative patients should have follow-up RPR titers at six and twelve months post-treatment. HIV-infected persons should have clinical and serologic follow-up at three, six, nine, 12, and 24 months post-treatment.3

**Jarisch-Herxheimer reaction**

The Jarisch-Herxheimer reaction is an acute febrile reaction frequently accompanied by headache, myalgia, fever, and other symptoms that usually occur within the first 24 hours after the initiation of any therapy for syphilis. It occurs most frequently among patients who have secondary syphilis, due to high bacterial burden. Patients should be informed about this possible adverse reaction. Many clinicians pre-treat with 1 g acethomopen in two hours prior to IM PCN, although this is not proven to prevent Jarisch-Herxheimer reaction.

**Treatment of Exposed Partners**

The CDC 2010 STD guidelines recommend that persons who were exposed within the 90 days preceding the diagnosis of primary, secondary, or early latent syphilis in a sex partner might be infected even if seronegative; therefore, such persons should be treated presumptively. Persons who were exposed >90 days before the diagnosis of primary, secondary, or early latent syphilis in a sex partner should be treated

### Table 2. Therapy for Early or Infectious Syphilis (Primary, Secondary and Early Latent)

<table>
<thead>
<tr>
<th>Recommended:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• IM Benzathine Penicillin G 2.4 MU x 1</td>
</tr>
<tr>
<td>For Penicillin-allergic patients1</td>
</tr>
<tr>
<td>• Doxycycline 100 mg po BID x 14 days</td>
</tr>
<tr>
<td>• Ceftriaxone 1 g IM or IV QD x 10-14 days</td>
</tr>
<tr>
<td>• Azithromycin 2 g orally x 1</td>
</tr>
</tbody>
</table>

1. Patients receiving non-penicillin regimens must have close clinical & serologic follow-up.
2. Little clinical support. Optimal dose & duration not defined. Treatment failures documented.
3. Do not use in pregnant women or MSM. Chromosomal mutations conferring resistance documented.

### Table 3. Take Home Points

- syphilis is in the differential of many common clinical syndromes
- always test for other STDs – HIV, gonorrhea, chlamydia
- rule out symptomatic neurosyphilis by careful H&P in all stages of syphilis
- in the absence of signs or sx of neurosyphilis, CSF exam does not change clinical outcome
- always obtain day of treatment RPR titer
- sexual contacts should be empirically treated or tested twice (initially and in 3 months)
presumptively if serologic test results are not available immediately and the opportunity for follow-up is uncertain.\(^{6}\)

**Reporting and follow-up**

All stages of syphilis are reportable diseases in RI, and laboratories report positive results directly to the RI Department of Health. Physicians are required to complete the RIDOH STD case report form (http://www.health.ri.gov/forms/reporting/cases/ SexuallyTransmittedDiseases.pdf), and Disease Intervention Specialists from the RI Dept of Health will interview index cases. Many index cases will decline to give names of sexual contacts, preferring to notify their contacts to be tested by their own physician. Importantly, RPR testing may be negative in incubating or early syphilis, therefore, contacts testing negative initially must be re-tested three months after their last exposure. Preferably, however, CDC recommends empirical therapy of all recent contacts, as noted above. Counseling Syphilis Fact Sheets for patients and contacts are available on the CDC website.\(^{22}\)

**Treatment Failure or Reinfection**

Signs or symptoms that persist or recur may suggest treatment failure or reinfection. The serologic definition of failure/reinfection is a sustained fourfold increase in RPR titer compared to the maximum or day of treatment titer. For this reason, it is imperative that a day of treatment titer be drawn, in addition to the initial blood draw that made the diagnosis. For treatment failure or reinfection, HIV testing should be repeated, and an evaluation for neurosyphilis, including lumbar puncture, should be performed.

The quantitative RPR/VDRL test should become nonreactive one year after successful therapy in primary syphilis and two years after successful therapy in secondary syphilis; most patients with late syphilis will be nonreactive by the fifth year after successful therapy.\(^{29}\) The RPR titer may fail to decline fourfold by one year post-treatment in 15-20% of patients. For these patients, CDC recommends repeat HIV testing, close clinical and serologic follow-up, and consideration of lumbar puncture to rule out inadequately treated neurosyphilis. If conversion to negative does not occur, and active syphilis is ruled out, the test result is said to be "sero-fast."\(^{7}\) It is unknown whether a serofast high titer has different clinical implication from a low titer.\(^{8}\)

**Conclusions**

Rising rates of infectious syphilis in Rhode Island, particularly among men who have sex with men, compels all physicians to be aware of the varied manifestation of this disease, and the management of the infected patient and contacts. Physicians must be mindful of the superiority of benzathine penicillin as the drug of choice for infectious syphilis, and the need for careful evaluation and follow-up for coexisting sexually acquired diseases.

**References**


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**Disclosure of Financial Interests**

The authors and/or their spouses/significant others have no financial interests to disclose.

**Discussion of Off-Label Usage**

Ceftriaxone, Azithromycin

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**Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG)** are the two most common reportable sexually transmitted infections (STIs) in the United States. Adolescent girls (15 to 19 years of age) and young women (20 to 24 years of age) are at highest risk for these infections. This likely reflects a combination of factors, including biological differences that place females at greater risk for STIs than males, as well as higher screening rates among young women. Similarly, men who have sex with men (MSM) are at increased risk for STIs including chlamydia and gonorrhea due to higher rates of unsafe sexual behaviors. Clinicians should be aware of current screening recommendations and diagnostic methods for detection of gonorrhea and chlamydia in genital as well as extra-genital sites to address this prevailing epidemic, particularly among younger women and MSM.

**Epidemiology in Rhode Island**

The surveillance data on chlamydia and gonorrhea in Rhode Island are available through 2010. Chlamydia is by far the most commonly reported STI in Rhode Island with a total of 3,480 cases (336 per 100,000 people; 2,478 females and 1,002 males) reported in 2010; this number is unchanged over the last five years. In contrast, reported cases of gonorrhea have decreased from 508 cases in 2006 (rate of 48.0 cases per 100,000) to 291 cases in 2010 (rate of 28.1 cases per 100,000), with rates unchanged since 2008. Females comprise 42% (121/291) of gonorrhea cases, compared to 71% of chlamydia cases (2,478/3,480). However, for both infections, rates are highest in 15 to 24 year olds among both males and females. By race and ethnicity, African-Americans are most disproportionately affected followed by Hispanics and non-Hispanic whites in Rhode Island.

**Clinical Presentation**

Over 50% of women with chlamydia infection are asymptomatic. The most common site of infection is the urogenital tract and, when symptomatic, usually manifests as cervicitis with mucoid vaginal discharge, bleeding, and dyspareunia. Ascending infection can present with right upper quadrant pain and/or pleuritic pain consistent with perihepatitis (Fitz-Hugh Curtis syndrome). Upper genital tract infection, otherwise known as pelvic inflammatory disease (PID), can present with vaginal discharge, dysuria, lower abdominal pain, and systemic symptoms such as fever. Chlamydia-induced PID carries a higher rate of infertility for women of child bearing age than gonorrhea. In pregnant women, undiagnosed infection can cause life threatening ectopic pregnancy, premature rupture of membranes, as well as neonatal conjunctivitis and/or pneumonia.

Pregnant women should be screened for all STIs.

As with their female counterparts, asymptomatic chlamydial infection is common among males, causing health care providers to frequently rely on screening tests in order to detect infection. Urogenital infection in men affecting the lower genital tract can present as a nongonococcal urethritis or epididymitis. Symptoms include dysuria and urethral mucopurulent discharge. Identification of infection in men is of importance as they can serve as a reservoir for infection in women.

Gonorrhea infections in females most commonly involve the cervix. Females are asymptomatic approximately half of the time. Typical symptoms include a mucopurulent discharge, and the exam may demonstrate friable cervical mucosa. Other symptoms may include abdominal pain, dyspareunia, dysuria, pruritus, PID, or perihepatitis. The main impetus for the early diagnosis and treatment of gonorrhea is to prevent the development of PID. Among women, gonococcal infections might not produce recognizable symptoms until complications such as PID have occurred. PID occurs in up to 40% of women with cervical infection, and can result in tubal scarring that can lead to ectopic pregnancy or infertility.

In men, gonorrhea is asymptomatic only 10% of the time. The majority of urethral infections caused by *N. gonorrhoeae* among men produce symptoms that cause them to seek curative treatment soon enough to prevent serious sequelae, but treatment might not be soon enough to prevent transmission to others. Gonorrhea usually causes urethritis including dysuria and a purulent penile discharge. Furthermore, gonorrhea usually does not cause other invasive disease in men, although it may progress to cause local abscesses, prostatitis, or epididymitis.

**Diagnostic Considerations**

The current standard laboratory test for detection of urogenital chlamydia and gonorrhea is a nucleic acid amplification test (NAAT). These tests are extremely sensitive and specific for detection of both organisms (>90%) using a noninvasive urine sample, thus reducing the need for pelvic examination or urethral sampling. These tests are FDA-cleared for the diagnosis of gonorrhea and chlamydia urogenital infections. Current guidelines recommend screening all women age 25 years or younger for chlamydia and gonorrhea, as well as women older than 25 who have a history of STIs, new or multiple sex partners, or exchange sex for drugs or money. Pregnant women should be screened for all STIs. Men with risk factors for infection should be screened.
including gay, bisexual, transgender, or other MSM. Screening for STIs including gonorrhea and chlamydia should occur for MSM on an annual basis, and more frequently if multiple or anonymous partners or intravenous drug use is involved (as often as three to six months).

Clinicians should be aware of extra-genital mucousal sites of infection for both gonorrhea and chlamydia, specifically the oropharynx and rectum. Anorectal gonorrhea infection in women is usually asymptomatic. Symptoms of proctitis such as anal pruritus, discharge, and pain on defecation are seen in a minority of patients (3%). For women, many infections occur in the setting of urethral, vaginal, or cervical infection (46%). However, anorectal infection may be found solely in the rectum (4-6%). It is unclear whether anal infection is due to anal intercourse or due to autoinfection from a urogenital source. Gonorrheal infection of the oropharynx is also common in women, occurring in 2-6% of individuals.\textsuperscript{10,11}

Among men and especially MSM, extra-genital sites of infection are common, and MSM are a high-risk group in which rates of STIs are increasing.\textsuperscript{12,13} Anorectal gonorrhea in men, compared to women, may be the only site of infection in up to 40%. Symptoms may include a purulent discharge, tenesmus, pain, and/or constipation. Infection may be due to gonorrhea alone, or may be in conjunction with other STIs including herpes simplex, chlamydia, and/or syphilis. Oropharyngeal infections are usually asymptomatic but can present with pharyngitis. Surveillance studies have suggested that the pharynx is the most common site of gonorrhea infection among MSM ranging from 3 to 15%.\textsuperscript{14,15} Interestingly, oropharyngeal gonorrhea is self-limiting with resolution of infection in the majority of cases. This may suggest that oropharyngeal treatment is unnecessary; however, the infection may be passed to the genital tract causing more invasive or disseminated disease.

Although no NAAT tests are FDA-cleared for use with rectal or oropharyngeal specimens for the diagnosis of gonorrhea and chlamydia, some laboratories have validated these specimen sites for clinical use.\textsuperscript{16} Cultures from these sites yield poor sensitivity at less than 50%. Over a 17 month period during 2011-2012, Lifespan laboratories tested a total of 32,589 and 31,201 samples for chlamydia and gonorrhea, respectively. (Table 1) Chlamydia was positive in 5.7% (111/19449) of urine specimens, (the most common specimen received for testing of CT and GC), 1.7% (5/291) of pharyngeal, and 11.8% (21/178) of rectal specimens. Gonorrhea was positive in 0.9% (159/17201) of urine, 3.4% (11320) of pharyngeal, and 5.3% (10/188) of rectal specimens. The high rates of oropharyngeal and rectal infections with both chlamydia and gonorrhea are consistent with previous studies demonstrating significant infection in patients selected for screening at these anatomic sites secondary to identification of risk factors.

**CONCLUSION**

Aggressive STI screening of the oropharynx, rectum, and urethra should be performed in individuals who perform sexual practices involving these sites, especially in MSM. Comprehensive STI screening for chlamydia and gonorrhea should include a NAAT of the urine, rectum (for men and women who have receptive anal intercourse), and the pharynx (for men with gonorrhea and women who have receptive oral intercourse). Recognition and diagnosis of chlamydia and gonorrhea is essential to decrease the morbidity associated with these diseases, as well as prevent the transmission of other STIs including HIV.\textsuperscript{16,17}

**REFERENCES**

3. Aggressive STI screening of the oropharynx, rectum, and urethra should be performed in individuals who perform sexual practices involving these sites, especially in MSM. Comprehensive STI screening for chlamydia and gonorrhea should include a NAAT of the urine, rectum (for men and women who have receptive anal intercourse), and the pharynx (for men with gonorrhea and women who have receptive oral intercourse). Recognition and diagnosis of chlamydia and gonorrhea is essential to decrease the morbidity associated with these diseases, as well as prevent the transmission of other STIs including HIV.

**Table 1: Anatomic site specific Chlamydia trachomatis and Neisseria gonorrhoeae infections as determined by nucleic acid amplification testing (NAAT).**

<table>
<thead>
<tr>
<th>Specimen Site</th>
<th>Total tested</th>
<th>Number positive</th>
<th>% positive of total</th>
<th>Total tested GC</th>
<th>Number positive</th>
<th>% positive of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>19449</td>
<td>1111</td>
<td>5.7</td>
<td>31201</td>
<td>159</td>
<td>0.9</td>
</tr>
<tr>
<td>Pharyngeal</td>
<td>291</td>
<td>5</td>
<td>1.7</td>
<td>320</td>
<td>11</td>
<td>3.4</td>
</tr>
<tr>
<td>Rectal</td>
<td>178</td>
<td>21</td>
<td>11.8</td>
<td>188</td>
<td>10</td>
<td>5.3</td>
</tr>
<tr>
<td>Total tested</td>
<td>32589</td>
<td></td>
<td></td>
<td>31201</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Diagnostic testing was with the Gen-Probe APTIMA Combo 2 assay over a time period of 17 months during 2011-2012. Validation of pharyngeal and rectal sites was performed by the Microbiology laboratory at Lifespan Laboratories.*

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Human Papillomavirus (HPV) and Trichomonas: Common, Concerning, and Challenging Sexually Transmitted Infections

Erna Milunka Kojic, MD

**Human papillomavirus (HPV) and Chlamydia**

Trichomonas are two of the most common sexually transmitted infections (STIs) in the United States and worldwide, with prevalences exceeding those of *Chlamydia* and *N. gonorrhoea* infections. Both infections have epidemiologic associations and can have serious health consequences.

**Human Papillomavirus (HPV) Infection**

HPV is the major cause of cervical and anal cancers, as well as oral and anogenital condylomas. HPV is a DNA virus of which over 90 types have been identified. Approximately 30 types are sexually transmitted and infect the anogenital area of both men and women. Data from the National Health and Nutrition Examination Survey have provided the first national estimate of the prevalence of HPV infection among women in the United States aged 14 to 59. Overall, 26.8 percent of women tested positive for one or more strains of HPV. Prevalence of HPV was highest in women ages 20-24. Among all participating women, the prevalence of high-risk types of HPV was 15.2 percent. The prevalence of HPV types 6, 11, 16, and 18—the types targeted by Quadrivalent HPV vaccine was 3.4 percent overall.

Persistence of high-risk types of HPV (16, 18, 31, 33, 35, 45) causes cervical dysplasia and cancer. Worldwide, types 16 and 18 account for the majority of cervical cancers, and one or more of these types can be found in 90% of high grade intraepithelial precursor lesions. Non-oncogenic types 6 and 11 are the etiologic agents for the majority of genital warts. Currently, cytology is used to screen for HPV related diseases. However, cytology as a cervical cancer screening method has a number of limitations, including the sensitivity to detect histologically significant disease. The sensitivity and specificity of cervical cytology ranges from 57% to 90% and from 65% to 97%, respectively. These limitations have led to a considerable interest in using a combination of high-risk HPV type testing and cytology for screening. The combined approach increases the sensitivity substantially compared with either test alone, and has a negative predictive value of 99% to 100%.

Studies with the HPV vaccine have demonstrated safety with relatively few adverse events reported.

Most women clear newly acquired HPV infection spontaneously, and the prevalence of HPV DNA positivity drops with age from a peak in adolescence and the early 20s. Current guidelines have therefore incorporated testing for high-risk HPV only for women 30 years of age and older, and triaging cervical cytology management based on HPV test results. In the absence of cervical lesions, treatment is not recommended for subclinical genital HPV infection or low grade lesions such as *cervical intraepithelial neoplasia* 1 (CIN1). In clinical care, no anti HPV treatment is available, only treatment of lesions caused by HPV infection. Preventing HPV infection is therefore important.

Currently, there are two prophylactic vaccines approved by the US Food and Drug Administration (FDA) for preventing HPV infection. These vaccines are a quadrivalent HPV vaccine (made by Merck and Co, and approved in June 2006) and a bivalent HPV vaccine (made by GlaxoSmithKline, and approved in October 2009). The quadrivalent vaccine is directed against HPV types 6, 11, 16, and 18 and is FDA-approved for preventing cervical cancer, genital warts, and precancerous or dysplastic genital lesions caused by HPV types 6, 11, 16, or 18. The bivalent vaccine is directed against HPV types 16 and 18 to prevent cervical cancer and precancerous lesions. Recommendations from the ACIP and the ACS are shown in Table 1.

Studies with the HPV vaccine have demonstrated safety with relatively few adverse events reported. The protective element of the vaccine is the high concentration of HPV type-specific neutralizing antibody. In the *Females United to Unilaterally Reduce Endo/Ectocervical Disease (FUTURE I/II)* study, almost all women who received the quadrivalent HPV vaccine became anti-HPV 6, 11, 16, and 18 seropositive one month after the third vaccine dose (99.8%, 99.8%, 99.8%, and 99.5% seropositive, respectively). The study also showed that the vaccine prevented 98-100% of CIN grades 1 to 3 or adenocarcinoma in situ, and vaginal, vulvar, perineal, and perianal intraepithelial lesions associated with vaccine-type HPV when administered to subjects who had not been previously exposed to HPV. The vaccine also reduced the rate of vulvar, vaginal, and perianal lesions by 34% and cervical lesions by 20% regardless of the type of HPV infection. The *FUTURE II* study showed that the efficacy of the vaccine in preventing HPV-16 and -18-related CIN 2 and 3 and adenocarcinoma in situ was lower (44%) for those women with previous exposure to the vaccine types.

In Rhode Island, state-supplied vaccine is available for routine vaccination at 11-12 years of age and catch-up vaccination for females 13-18 years of age. As of July 2010, the state also began supplying the vaccine for permissive use in males nine through 18 years of through the universal state-supplied vaccine program. Vaccine recommendations from both the ACIP and the American Cancer Society are shown in Table 1.

**HPV and HIV co-infection**

Highly active antiretroviral regimens have revolutionized the treatment of...
individuals infected with HIV and have resulted in dramatic reductions in morbidity and mortality. While mortality due to HIV infection or AIDS declined, mortality due to malignancies has increased and now represents an increasing proportion of overall deaths among persons with HIV infection. HPV infections are more prevalent and persistent in HIV-infected women, with a prevalence of 64% compared to 28% in HIV-uninfected women. HIV-infected women have been reported to have a higher prevalence and persistence of HPV infection and to have an increased risk for abnormal Papanicolaou (Pap) smears as well as cervical cancer. Therefore, the burden of HPV infection is greater among HIV-infected rather than HIV-uninfected women.

A concern in HIV-infected women is the high prevalence of previous exposure to HPV 6, 11, 16 and 18 would decrease the vaccine’s efficacy. One study, evaluating 767 HIV-infected and 390 uninfected women, the DNA prevalence of one or more of HPV types 6, 11, 16, and 18 was 15.9%; specifically, type 6 was 3.1%, 11 was 0.9%, 16 was 5.7%, and 18 was 6.1% (6.7% in HIV-uninfected women). Thus, although HIV-infected women have a much higher prevalence of these four types than HIV-uninfected women, the majority of them (84-89%) did not have the types contained in the vaccine. Preventing infection of the four vaccine HPV types could decrease the impact of HPV infection among HIV-infected individuals. The immunogenicity and safety of an HPV vaccine in HIV-infected women is being evaluated.

In terms of managing HPV related diseases in HIV infected women, the American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines recommend that HIV-infected women be managed in the same manner as women in the general population. At present, insufficient data are available to support the use of HPV testing for triage of HIV-seropositive women aged 30 years and older. Based on the lack of sufficient data, the DHHS guidelines recommend a referral for colposcopy for any cervical cytologic abnormality found in HIV-seropositive women, regardless of the presence or absence of high-risk HPV types.

### Table 1. Comparison of Advisory Committee on Immunization Practices and American Cancer Society Recommendations for Human Papilloma Virus (HPV) Vaccination

<table>
<thead>
<tr>
<th>Advisory Committee on Immunization Practices</th>
<th>American Cancer Society</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quadrivalent HPV vaccine: Routine HPV vaccination with 3 doses of vaccine is recommended for girls AND boys 11 and 12 years of age with catch-up for females and males aged 13 to 26 years if not vaccinated previously or have not completed the series.</td>
<td>Quadrivalent or bivalent HPV vaccine: Routine HPV vaccination with 3 doses of vaccine is recommended for girls 11 and 12 years of age with catch-up for girls aged 13 to 18 years if not vaccinated previously or have not completed the series.</td>
</tr>
<tr>
<td>Bivalent HPV vaccine: Routine HPV vaccination with 3 doses of vaccine is recommended for girls 11 and 12 years of age with catch-up for girls and women aged 13 to 26 years if not vaccinated previously.</td>
<td>Bivalent HPV vaccine: Girls as young as 9 years of age can be vaccinated.</td>
</tr>
<tr>
<td>Quadrivalent or bivalent HPV vaccine: Girls as young as 9 years of age can be vaccinated.</td>
<td>Quadrivalent or bivalent HPV vaccine: Girls as young as 9 years of age can be vaccinated.</td>
</tr>
<tr>
<td>Quadrivalent HPV vaccination is recommended for all female and male individuals 13 through 26 years of age.</td>
<td>Quadrivalent or bivalent HPV vaccine: HPV vaccination is recommended for all females 13 through 18 years of age.</td>
</tr>
<tr>
<td>Bivalent HPV vaccine is recommended for all girls and women 13 through 26 years of age.</td>
<td>The American Cancer Society has no recommendation regarding the use of either HPV vaccine in men and boys.</td>
</tr>
<tr>
<td>Quadrivalent or bivalent HPV vaccine: The vaccine is not licensed for use in girls younger than 9 years of age or women older than 26 years of age. Quadrivalent HPV vaccine is contraindicated for persons with a history of immediate hypersensitivity to yeast. Bivalent HPV vaccine in prefilled syringes is contraindicated for persons with anaphylactic latex allergy.</td>
<td>Data are insufficient to recommend for or against universal vaccination of women 19 to 26 years of age. HPV vaccination is not recommended for women older than 26 years of age.</td>
</tr>
</tbody>
</table>

### Trichomonas vaginalis Infection

*Trichomonas vaginalis* (*T. vaginalis*) is a sexually transmitted protozoan parasite. In the United States, an estimated 3.7 million people have the infection, but only a third develops any symptoms of trichomoniasis. In a nationally representative sample, the prevalence of trichomoniasis among 14–49-year-old women in the United States was 3.1%, corresponding to 2.3 million women with trichomoniasis compared with a prevalence of 0.33% and 2.5% for Neisseria gonorrhoea and Chlamydia trachomatis infections respectively (NHANES). Infection is more common in women than in men, especially non-Hispanic black women, and older women are more likely than younger women to have been infected. The prevalence is likely to be underestimated as the infection is not reportable like many other STIs, available.
diagnostic methods are often insensitive, and the clinical awareness of the infection is often limited to women and not their male partners. The symptoms of \( T.\ vaginalis \) infection are less pronounced in men, and the detection of infection is more complicated. Studies of male STD clinic patient populations have reported prevalences between 11 and 17%. The prevalence of \( T.\ vaginalis \) among male sexual partners of infected women is over 73%.

Males with \( T.\ vaginalis \) infections are often untreated, both because of lack of symptoms and due to lack of treatment as male partners of women with known \( T.\ vaginalis \). \( T.\ vaginalis \) re-infection among women is therefore common.

\( T.\ vaginalis \) causes vaginitis, pelvic inflammatory disease, and several adverse obstetric sequelae (e.g., premature rupture of membranes, low birth weight, preterm labor). Recent advances in TV diagnostics have led to an improved understanding of the epidemiology of this pathogen. \( T.\ vaginalis \) is also associated with prolonged HPV carriage and increased risk of acquiring HIV infection. Studies have suggested that \( T.\ vaginalis \) may increase the rate of HIV transmission by approximately twofold.

This fact can translate into a significant problem in light of the high \( T.\ vaginalis \) prevalence globally.

Until recently, lack of sufficiently sensitive and specific diagnostic tests has limited the accurate diagnosis and recognition of this infection. Diagnosis of vaginal trichomoniasis can be done by microscopy of vaginal secretions (wet mount), culture, rapid antigen detection, and nucleic amplification tests (NAAT). Microscopy detection is highly insensitive in detecting \( T.\ vaginalis \) and culture is time consuming. There are several nucleic acid tests available although only one, the Affirm VP III hybridization assay, has been FDA approved. Other commercially available tests like the Gen-Probe Aptima \( T.\ vaginalis \) transcription-mediated amplification (TMA) tests are being evaluated and may be even more sensitive in detecting \( T.\ vaginalis \).

With increasing evidence of complications associated with trichomonas infections, screening for \( T.\ vaginalis \) should be encouraged, especially as treatment with metronidazole 2 gm or tinidazole 2 gm in single doses is easy and highly effective.
Testing and Treatment After Non-Occupational Exposures To STDs and HIV

Erica J. Hardy, MD, MA, MMSc

WOMEN MAY PRESENT TO AN EMERGENCY room, a dedicated Sexually Transmitted Disease (STD) clinic, or their primary care provider with concern for a STD including Human Immunodeficiency Virus (HIV) after a sexual exposure. The goal of this review is to provide an overview of current recommendations for the prophylaxis, testing, and treatment of the adult patient for STDs and HIV after a sexual exposure, including sexual assault. Issues surrounding appropriate referral, follow up care, and emergency contraception will also be addressed. Recently updated recommendations for the treatment of sexually transmitted infections, as well as recommendations for antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV are available from the Centers for Disease Control and Prevention.1,2 These guidelines, as well as other recent data and expert opinion form the basis of this review.

CASE
A 20 year old primary care patient is a sophomore in college and is currently home for the summer. She calls the office for an urgent visit. When you see her that afternoon, she reports that 2 days prior, she was at a party with some friends from high school, and that evening she had sexual intercourse with a male acquaintance. No condom was used, and she is worried that she may have acquired a sexually transmitted infection. She requests “STD testing.” What questions should you ask?

Important questions in the history of a sexual exposure to a possible STD including HIV:
• Were you forced to have this sexual contact? Did you feel unsafe? (Assesses for sexual assault in which case more urgent referral for evidence collection may be needed.)

TESTING VERUS EMPIRIC TREATMENT AFTER SEXUAL EXPOSURE

“What do I need to be tested or treated for STDs?”

While according to the recent recommendations of the CDC, both options are acceptable, most experts recommend empiric treatment after exposure, especially in the context of sexual assault. Infection may not be established immediately after exposure, so depending on the time from exposure to presentation for medical care, enough time may not have elapsed for a STD test to be positive. In addition, follow up can be poor in many patients and the opportunity for treatment and therefore potentially preventing further exposures may be lost. If testing in the absence of empiric treatment is employed, then testing should not be guided by symptoms alone, as many STDs may be asymptomatic and yet still have the potential to cause significant morbidity and transmission to others.3

RECOMMENDATIONS FOR PROPHYLAXIS/TREATMENT OF STDs AFTER A SEXUAL EXPOSURE

“What medications will I need to take?”

The CDC has published recommendations for treatment to prevent sexually transmitted infections after a sexual exposure, including gonorrhea, chlamydia, trichomonas, as well as hepatitis B and HIV.1 In the adult patient, empiric treatment, rather than testing (unless symptoms are present) is recommended by most experts. Syphilis is less prevalent, however, depending on the population, empiric treatment might be appropriate. Treatment for gonorrhea with ceftriaxone also likely will treat incubating syphilis.

The regimens recommended for empiric treatment of bacterial STDs after a sexual exposure are as follows:
• For Chlamydia: azithromycin 1000mg orally in a single dose (alternative: doxycycline 100mg orally twice a day for seven days—doxycycline is relatively contraindicated in pregnancy and in children less than eight years old).

• For Gonorrhea: ceftriaxone 250mg intramuscularly in a single dose (alternative to ceftriaxone not an option: cefixime 400mg orally in a single dose; alternative in the severely penicillin allergic patient, azithromycin 2000mg orally in a single dose although there are concerns with emergence of resistance with azithromycin). Quinolones are no longer recommended for the treatment of gonorrhea due to unacceptable levels of resistance.

• For Trichomonas: metronidazole 1gm orally in a single dose (avoid use with alcohol). (A single dose of metronidazole is no longer considered adequate for the treatment of bacterial vaginosis, in which case a longer course is required).1

**Recommendations for follow-up testing for bacterial STDs**

“How do I prevent pregnancy?”

Progestin-only emergency contraception has been shown to be 98.5% effective in preventing pregnancy if taken within 120 hours after unprotected intercourse. It should be taken as soon as possible after the exposure as efficacy likely decreases with time. It should not be given if a patient is already pregnant, but there is no evidence that it causes abortion or harm to the pregnancy if given in an already established pregnancy. Emergency contraception (Plan B, and others) is available for purchase in a pharmacy without a prescription for women and men 17 years of age or older.

• Dose = levonorgestrel or Plan B (1.5mg orally in a one time dose, taken up to 120 hours after unprotected intercourse)

**Risks of HIV Transmission after Sexual Exposure**

“What are my chances of getting HIV?”

Risk of HIV acquisition after sexual exposure, like the risk of other STDs, depends on characteristics of the exposure and of the source patient.

**Hepatitis B**

- If the patient is unvaccinated or known not to have responded to a complete Hepatitis B vaccine series, AND exposed to a source known to be Hepatitis B infected: 1) Hepatitis B Immunoglobulin in a one time intramuscular dose of 0.05mL/kg (ideally within 14 days of a sexual exposure); AND 2) administer Hepatitis B vaccine series.

- If the patient is unvaccinated or known not to have responded to a complete Hepatitis B vaccine series, AND exposed to a source with an unknown Hepatitis B status: Initiate the Hepatitis B vaccine series if not already vaccinated and/or immune, with first dose given as soon as possible, but ideally within 14 days of exposure.

- Pregnancy is not a contraindication to Hepatitis B vaccination if otherwise indicated.

**Hepatitis C**

Sexual transmission of Hepatitis C was thought to occur rarely, however, there have been more recent reports of sexual transmission occurring, especially among HIV-infected persons and men who have sex with men. The CDC reported that 10% of individuals with acute hepatitis C reported contact with a known HCV-infected sex partner as their only risk factor for infection.4 The risk for acquisition of hepatitis C increases with the number of sexual partners, especially of those sex partners are co-infected with HIV.

There is no effective postexposure prophylaxis against hepatitis C at this time and viral kinetics suggest that established infection is necessary for treatment to work. Because of this, follow up testing after possible exposure is important in order to identify acute or early infection, the treatment of which may have better outcomes.7 Suggested timing of follow up testing for hepatitis C (with HCV antibodies and HCV RNA) should be at six weeks and again at three months after sexual exposure.

**Pregnancy Prevention after Sexual Exposure**

“How do I prevent pregnancy?”

Empiric treatment is generally recommended, and if administered appropriately, follow up testing is not needed in the absence of symptoms. Re-testing is recommended in the following situations:

• Signs of symptoms of infection (such as vaginal or penile discharge).

• Patient requests testing (as they may have had another exposure of which the provider is unaware).

• Initial treatment (all or part) was omitted or refused by the patient. In this case testing should be performed approximately two weeks after the exposure. Samples should be collected from all areas that were exposed (e.g., vagina, rectum, and/or pharynx).

**Recommendations for the Prevention of Hepatitis B and C after a Sexual Exposure**

“Do I need to worry about Hepatitis?”
be slightly lower at 0.06%, and the risk from oral sex is likely substantially lower, although not zero. Sexual assault may increase transmission risk compared to consensual sex.

The risk of HIV transmission and whether to offer HIV postexposure prophylaxis also depends on whether the source patient has HIV. Characteristics of the source patient that increase the risk of HIV would be men who have sex with men, persons with multiple sexual partners, intravenous drug users, commercial sex workers, persons with concomitant genital ulcer disease, those with a history of incarceration, or those from an area with an HIV prevalence of 1% or more. The HIV seroprevalence has been evaluated in several special populations. In a Rhode Island inmate population, the HIV seroprevalence was 1% in sexual assailants, 3% in the prison population, compared to 0.3% in the general male population of the state.

**HIV POSTEXPOSURE PROPHYLAXIS (PEP) AFTER SEXUAL EXPOSURE**

**Is there medication I can take to prevent HIV?**

Postexposure prophylaxis therapy with a 28 day course of antiretroviral medications after exposure to HIV has gained widespread acceptance despite lack of efficacy data in the setting of sexual exposure. In 2005, the CDC developed recommendations for its use, and several states have consensus guidelines for HIV PEP; however as the HIV treatment field expands, specific regimens used in practice may change before guidelines are updated. Its efficacy is extrapolated from animal data, from a study of healthcare workers who were given zidovudine after a needlestick injury which reduced the risk of HIV acquisition by 81%, from the success of reducing which reduced the risk of HIV infection after a needlestick injury given zidovudine after a needlestick injury. A study of healthcare workers who were given antiretrovirals prior to HIV exposure to prevent HIV infection in high risk groups appears promising. HIV PEP may be warranted if the following criteria are met:

- A significant exposure has occurred (exposure of the vagina, rectum or any mucous membrane to potentially infectious blood, semen, or vaginal/rectal secretions) AND
- The patient presents within 72 hours of the exposure AND
- The source patient is known to be HIV infected or HIV status is unknown but is at high risk of being HIV infected (as in risk groups outlined above). HIV PEP may be considered in other cases where the source patient’s HIV status is unknown or is at lower risk of HIV on a case-by-case basis. In which case the source patient’s treatment history, if known, must be taken into consideration with the assistance of an HIV treatment specialist when devising a PEP regimen

The specific regimens for HIV postexposure prophylaxis is beyond the scope of this review, however in general, two nucleoside reverse transcriptase inhibitors are used with the possible addition of a protease inhibitor in higher risk exposures, extrapolating from HIV treatment data.

If HIV PEP is to be initiated, then an HIV test should be performed at baseline (to avoid initiating PEP in an HIV infected patient). Follow up HIV testing should be performed at 6 weeks, 3 months, and 6 months after exposure, whether or not HIV PEP was initiated.

**A NOTE ABOUT SEXUAL ASSAULT**

In Rhode Island, it is estimated that one in eight women have been sexually assaulted during their lifetime. Rape occurs in men as well, although the prevalence is likely lower based on other population studies. If an adult patient presents after a sexual assault and wishes to have evidence collection, they should be referred to a local emergency room for evaluation and evidence collection, as well as STD and HIV PEP if indicated. College health services can often provide many of these services, although not evidence collection. The time limits for evidence collection vary by jurisdiction and range from 72-120 hours (96 hours in Rhode Island).

**Summary**

Sexual exposure to STDs including HIV and hepatitis is common. Sexual assault is also prevalent and should be screened for in a patient presenting for medical care after potential sexual exposure to STDs. Primary care providers should be familiar with current recommendations for STD prophylaxis and treatment after sexual exposure to STDs, and be aware that HIV postexposure prophylaxis is effective and available if indicated after sexual exposure to HIV. Providers should also be aware of the need for prompt referral for evaluation and medical care of the adult patient after a sexual assault.

**References**

postexposure prophylaxis guidelines for Rhode Island healthcare practitioners. 2002.

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The author and/or their spouse/significant other have no financial interests to disclose.

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Maternal Smoking and Birth Defects in Rhode Island

William Arias, MPH, and Samara Viner-Brown, MS

Cigarette smoking has long been associated with poor neonatal conditions such as premature birth and sudden infant death syndrome. Many studies have also shown a link between maternal smoking and congenital anomalies. Pregnant women who smoke are at greater risk for having a baby with a neural tube defect, clubfoot, craniosynostosis and congenital heart defects. To follow up on these studies, the Rhode Island Birth Defects Program has examined whether the same relationship exists between maternal smoking and birth defects in Rhode Island.

Methods
This case-control study included live births that occurred in Rhode Island during 2007-2010 among Rhode Island residents. Cases represented newborns with at least one birth defect that were discharged from Women & Infants and Kent hospitals (representing about 80% of the Rhode Island live birth population). A birth defect in Rhode Island is primarily defined as any condition with ICD-9 (International Statistical Classification of Diseases, 9th Edition) codes 740-759.9 and 760.71. Controls were selected using systematic random sampling of newborns from vital records. Smoking exposure among cases was determined by self-reported number of cigarettes smoked per day during pregnancy noted in prenatal records and captured through routine birth defects risk factor surveillance. Smoking exposure among controls was determined by the number of cigarettes smoked per day during pregnancy, which is self-reported on the birth certificate worksheet in vital records. Controls were cross-linked with birth defects cases using their vital record identification number to avoid duplication of study subjects.

Birth defects selected for the study were clubfoot, cryptochidism, cleft/lip palate, pulmonary stenosis, and hypoplastic left heart syndrome. Selected infant and maternal characteristics were used to identify differences in populations for subsequent regression analysis. Frequency and percentages of infant and maternal characteristics were calculated for the case and control populations. Logistic regression was used to measure the exposure-outcome association controlling for gestational age, infant sex, maternal race/ethnicity, city/town of residence, marital status, and for the specific birth defects Down syndrome and amniotic banding. Adjusting for Down syndrome as a potential confounder was necessary to control for the relationship between the chromosomal disorder and congenital heart defects. Births with gestational ages less than 36 weeks were defined as preterm for this study. Core cities are communities where 15% or more of children live in poverty.

Results
During 2007-2010, 1,676 birth defects cases were included in the study. Among the 2007-2010 live birth population (n = 44,732), 3,267 (7.3%) were selected as study controls. Table 1 shows the selected infant and maternal population characteristics.

Table 1. Demographic Characteristics of Study Cases and Controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases (n=1876)</th>
<th>Controls (n = 3267)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoker (at least 1 cig/day)</td>
<td>Yes 211 (12.6)</td>
<td>No 1485 (87.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple Birth</td>
<td>Yes 21 (1.3)</td>
<td>No 1655 (98.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational Age*</td>
<td>Preterm 337 (20.1)</td>
<td>Term 1338 (79.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infant Sex</td>
<td>Male 1030 (61.5)</td>
<td>Female 646 (38.5)</td>
</tr>
<tr>
<td></td>
<td></td>
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</tr>
<tr>
<td>Maternal Age</td>
<td>&lt; 20 178 (10.6)</td>
<td>No 331 (10.1)</td>
</tr>
<tr>
<td></td>
<td>20-34 1182 (70.5)</td>
<td>No 2401 (73.5)</td>
</tr>
<tr>
<td></td>
<td>&gt; 35 316 (18.9)</td>
<td>No 535 (16.4)</td>
</tr>
<tr>
<td>Core City**</td>
<td>Yes 896 (53.5)</td>
<td>No 1591 (48.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Race/Ethnicity</td>
<td>White 947 (56.7)</td>
<td>Black 217 (13.0)</td>
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<td></td>
<td>Hispanic 404 (24.2)</td>
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<td></td>
<td>Asian 62 (3.7)</td>
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<tr>
<td>Marital Status</td>
<td>Not Married 843 (50.3)</td>
<td>Married 833 (49.7)</td>
</tr>
</tbody>
</table>

* Preterm birth is defined as a gestational age <36 weeks for this study
** Core city is defined as a community where 15% or more of children live in poverty
of cases and controls for RI live births. There were 211 (12.6%) cases and 315 (9.6%) controls with maternal smoking exposure of at least one cigarette/day. There were notable differences between the case and control populations regarding gestational age and infant sex. Specifically, 20.1% of the cases were considered premature compared to 10.3% of the controls. The male-to-female ratio among cases was higher (1.6:1) than the male-to-female ratio among controls (1:1).

Table 2 shows the association between maternal smoking and selected birth defects in Rhode Island, adjusting for selected infant and maternal characteristics, Down syndrome, and amniotic banding. There was a significant association between maternal smoking and all birth defects (aOR = 1.27). Specifically, there were strong, significant associations between maternal smoking and clubfoot (aOR = 2.24), and pulmonic stenosis (aOR = 4.75). Although a positive association existed between maternal smoking and cleft lip/palate (aOR = 1.23) and cryptorchidism (aOR = 1.14), there was no statistical significance. There were no hypoplastic left heart syndrome cases found with maternal smoking exposure of at least one cigarette/day.

**DISCUSSION**

Results from this study show that women who smoked during pregnancy were more likely to give birth to a child with clubfoot or pulmonary stenosis, compared to women who did not smoke. Pulmonic stenosis is a diagnosis typically caused by stenosis of the pulmonary artery, a narrowing of the arteries in the lungs. It can also be caused by a defective pulmonary valve in the heart (pulmonary valve stenosis), but there were an insufficient number of cases in Rhode Island to measure this condition with maternal smoking. A significant number of pulmonic stenosis cases associated with cigarette smoking were found recently in 2009-2010 in Rhode Island, and the RI Birth Defects Program is continuing to monitor this condition.

This study also demonstrated a stronger relationship between clubfoot and maternal smoking than has been identified in previous studies. A recent chart review of clubfoot cases showed no diagnoses for amniotic bands (another cause of clubfoot) 6. By the end of the first trimester, the foot of the fetus changes to a slight equinovarus adductus position, where the influence of chemicals in cigarettes can produce a permanent arrest throughout the fetal stages 7. Although aggregating four years of Rhode Island birth defects data helped increase the power of the study, the sample size was still low for cleft lip/palate (n = 32), another condition that has been linked with maternal smoking 8.

There were other limitations to this study. Pierre-Robin syndrome, a known syndrome associated with cleft lip/palate, was not adjusted for regression analysis. Another limitation is that smoking exposure is based on self-report. However, limiting the definition of smoking exposure to “number of cigarettes smoked per day” reduced response bias (records of mothers reporting number of cigarettes smoked per day during pregnancy is likely to be similar between case and control groups than mothers reporting overall smoking during pregnancy without noted number of cigarettes smoked). Another limitation is sample size, which not only limits analysis for congenital heart defects and other anomalies linked with maternal smoking but also limits analysis for a potential exposure-dose relationship.

This study shows that there is a strong relationship between maternal smoking and clubfoot and pulmonary stenosis, although a larger sample size is needed to better understand this relationship with cleft lip/palate. Nevertheless, this study adds further justification for increased tobacco control and prevention among pregnant women to help reduce birth defects in Rhode Island.

**REFERENCES**


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**Disclosure of Financial Interests**

The authors and/or their spouses/significant others have no financial interests to disclose.

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LARYNGEAL CHONDROSARCOMA IS A RARE RELATIVELY SLOW-GROWING tumor arising from the laryngeal cartilages. The slowly progressive nature of symptoms means that many patients will undergo multiple diagnostic studies, and recognition of the imaging characteristics of the tumor may assist significantly in diagnosis. We present a case of a laryngeal chondrosarcoma lacking the calcifications which are often a diagnostic clue.

CASE REPORT
A 67-year old male presented with complaints of progressive hoarseness and stridor. The patient first noticed hoarseness of the voice five months prior to presentation at which time he was evaluated with CT of the neck (Figure 1), which was unremarkable. He also underwent direct laryngoscopy which revealed normal cords without lesions and normal movement. The hoarseness continued and a repeat CT was obtained 3 months later, which showed mildly increased prominence of the soft tissues in the posterior subglottic trachea. The patient then underwent rigid laryngoscopy under general sedation which showed mild supraglottic edema, but normal appearing cords with normal movement. Supraglottic and posterior laryngeal biopsies were done which showed hyperplastic squamous epithelium with keratosis.

Three days after his procedure the patient complained of shortness of breath, dyspnea, stridor, dysphagia, and drooling and presented to the ED for evaluation. Flexible laryngoscopy showed mobile cords with edema, and inability to evaluate the subglottic area.

Chest radiography was unremarkable. CT of the neck with IV contrast showed abnormal soft tissue in the posterior aspect of the subglottic trachea surrounding the cricoid cartilage, with mild airway narrowing (Figure 2). There was no evidence of abnormal lymphadenopathy, and the visualized thyroid appeared normal.

Given his ongoing respiratory distress in the setting of an obstructing mass lesion, the patient underwent urgent tracheostomy in order to secure his airway. Biopsies were taken at the time of the procedure as well as by flexible bronchoscopy several days later. These revealed areas of acute inflammation and surface ulceration, as well as fragments of atypical cartilage, with enlarged chondrocytes, irregularly distributed on a basophilic matrix. The atypical chondrocytes demonstrated hypercellularity, nuclear hyperchromasia, and occasional binucleated forms (Figure 3); consistent with a diagnosis of laryngeal chondrosarcoma.

The patient subsequently underwent total laryngectomy, and all margins were clear of residual tumor. Review of the surgical specimen showed a well delineated posterior chondrosarcoma measuring 3.8 x 1.0 x 1.2 cm arising from the cricoid cartilage (Figure 4), and the examining pathologist noted that the “airway was narrow and rigid, barely allowing for the passage of the smallest finger.” After recovery from surgery, the patient is doing well with no evidence of residual disease.

DISCUSSION
Chondrosarcoma is a common tumor of bone, which very uncommonly presents in the larynx. While chondrosarcomas are the 3rd most common tumor of bone1, and the most com-
chondrosarcoma diagnosed in patients over 50 years of age, they represent only about 0.5% of all laryngeal tumors, although estimates of incidence are complicated by confusion with laryngeal chondromas, and certain other rare clinical entities. The pathogenesis of these tumors is not well understood although there has been speculation about the possibility that they arise from disordered ossification of laryngeal cartilages, or ischemic degeneration of pre-existing benign chondromas.

The mean age of presentation of laryngeal chondrosarcoma is the mid-sixth decade of life; and although most series have found a male predominance, there does not appear to be any significant age difference at presentation between the genders. Most patients have symptoms attributable to vocal cord dysfunction or direct compression of the larynx such as hoarseness, dyspnea, and dysphagia. Similar to this case, almost all patients have a prolonged duration of symptoms prior to diagnosis, with a mean duration of 28 months in the largest published series.

Radiographic studies generally show mass lesions of mixed density with hypodense, isodense, and hyperdense areas compared to surrounding muscle. The mass is usually well-defined, with displacement, replacement and destruction of surrounding cartilaginous structures. Invasion of vascular structures is rare. Reports describe a range of fine punctuate to stippled coarse (“popcorn”) calcifications, seen in 75-80% of reported cases, although this feature was lacking in our patient.

Pathologically, most laryngeal chondrosarcomas arise from the cricoid cartilage, as in this case, although the other laryngeal cartilages can be also be involved. At time of resection the tumor is usually described as lobular, blue-gray, and “glistening”. Microscopically, chondrosarcomas are defined by loss of normal cartilaginous structure and distribution of chondrocytes in basophilic to metachromatic matrix. Grading of chondrosarcomas is divided by degree of invasion, cell irregularity, and the presence of multinucleate cells, and nuclear hyperchromasia.

Laryngeal chondrosarcomas are generally considered to be relatively slow growing and nonaggressive tumors, although their location can make management difficult. Conservative larynx-sparing surgery is usually attempted when possible, and conservative surgery does not generally negatively impact survival. Chemotherapy and radiation are not generally effective modalities, although case reports of primary or adjuvant radiation therapy exist. The rate of metastatic disease varies by reported series between 2-10%, and death from laryngeal chondrosarcoma is rare with survival rates of 90% or greater.

REFERENCES
6. Fletcher, CDM, Unni, KK, Mertens, F. (eds.) Pathology and Genetics of Tumours of Soft Tissue and Bone. 2002. Lyon, France: IARC.

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Information for Contributors

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**Contributions**
Contributions report on an issue of interest to clinicians in Rhode Island: new research, treatment options, collaborative interventions, review of controversies. Maximum length: 2500 words. Maximum number of references: 15. Tables, charts and figures should be submitted as separate electronic files (jpeg, tif, or pdf). Each submission should also be accompanied by a short (100-150 words) abstract.

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Clinicians are invited to describe cases that defy textbook analysis. Maximum length: 1200 words. Maximum number of references: 6. Photographs, charts and figures may accompany the case.

**Point of View**
Readers share their perspective on any issue facing clinicians (e.g., ethics, health care policy, relationships with patients). Maximum length: 1200 words.

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Authors discuss new treatments. Maximum length: 1200 words.

**Advances in Laboratory Medicine**
Authors discuss a new laboratory technique. Maximum length: 1200 words.

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Authors submit an interesting Image, with a 300-400 word explanation.

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Physician’s Lexicon
The Florid Eponyms of Medicine

Dreams of immortality are rarely a conscious element in the stressful lives of physicians. Just getting through each day without adding measurably to one’s list of problems is a sufficient objective for most of us. It is rare, then, for a physician’s name to be perpetuated beyond his obituary notices except if an ailment (e.g., Bright’s Disease), a clinical sign (e.g., Babinski Sign), a vaccine (e.g., Salk polio vaccine) or a type of neurological abnormality (e.g., Jacksonian seizure) bears his name.

Physicians don’t have mountains, rivers or other major geographic sites named after them. But in one small scientific endeavor, the names of physicians used as eponyms, predominates: the field of ornamental flowers. This was no accident of fate since botany and medicine were inextricably intermixed until recent centuries. And, accordingly, so many trained physicians of prior centuries were also botanists seeking naturally-occurring pharmaceuticals to be employed as empiric remedies for their patients.

Consider how many of the currently enjoyed flowers bear the name – sometimes slightly modified – of practicing physicians. Leonhard Fuchs, born in Bavaria in 1501, was professor of medicine at Tubingen University. He was one of the first to describe the therapeutic effects of foxglove. And the *fuchsia* is named in his honor.

Matthias de Lobel, a 16th Century native of France, emigrated to England, eventually becoming court physician to James I. The *lobelia* is named after him. Pierre Magnol born in 1638, and professor of medicine at Montpellier, was France’s most eminent botanist in the 17th Century, is immortalized in the *magnolia*.

Geore Camellus, a 17th Century missionary-physician-botanist, is remembered through the *camellia*. Olaf Rudbeck, Sweden’s great physician botanist (and mentor to Carolus Linnaeus) has given his name to the *rudbeckia*. And yet another Swedish physician, Anders Dahl (a student of Linnaeus) is immortalized in the *dahlia*.

Caspar Wistar, born in Philadelphia in 1761, taught medicine at University of Pennsylvania, created what is now the Wistar Institute, and had the *wisteria* plants named after him. And one should not forget Joel Poinsett of South Carolina, Madison’s roving ambassador, world traveler, botanist and later, congressman has his name given to the *poinsettia* plants.

Few of these physician-botanists are remembered today in the formal annals of medicine. Yet they have been truly immortalized in the naming of many actively enjoyed plants. Given a choice, would any aspiring physician wish to be remembered as a form of gout or, alternatively, as a glorious blossom such as the magnolia?

– Stanley M. Aronson, MD

VITAL STATISTICS

Edited by Colleen Fontana, State Registrar

Rhode Island Monthly Vital Statistics Report
Provisional Occurrence
Data from the Division of Vital Records

<table>
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<th>Underlying Cause of Death</th>
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<tr>
<td>Cerebrovascular Diseases</td>
<td>36</td>
</tr>
<tr>
<td>Injuries (Accidents/Suicide/Homicide)</td>
<td>65</td>
</tr>
<tr>
<td>COPD</td>
<td>46</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vital Events</th>
<th>Reporting Period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>February 2012</td>
</tr>
<tr>
<td></td>
<td>Number</td>
</tr>
<tr>
<td>Live Births</td>
<td>925</td>
</tr>
<tr>
<td>Deaths</td>
<td>840</td>
</tr>
<tr>
<td>Infant Deaths</td>
<td>(11)</td>
</tr>
<tr>
<td>Neonatal Deaths</td>
<td>(10)</td>
</tr>
<tr>
<td>Marriages</td>
<td>278</td>
</tr>
<tr>
<td>Divorces</td>
<td>269</td>
</tr>
<tr>
<td>Induced Terminations</td>
<td>359</td>
</tr>
<tr>
<td>Spontaneous Fetal Deaths</td>
<td>56</td>
</tr>
<tr>
<td>Under 20 weeks gestation</td>
<td>(51)</td>
</tr>
<tr>
<td>20+ weeks gestation</td>
<td>(5)</td>
</tr>
</tbody>
</table>

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 estimated population of 1,052,567. (www.census.gov)

(c) Years of Potential Life Lost (YPLL).

Note: Totals represent vital events that occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

* Rates per 1,000 estimated population
# Rates per 1,000 live births
**Ninety Years Ago, August, 1922**

W.T. Buffum, Jr., MD, examines rickets and tetany in infancy beginning by a characterization of rickets as softening and deformities in the bony structure, malnutrition, anemia, and weakness of the voluntary and involuntary muscles which interferes with development and resistance to intercurrent disease, and noting that when recovery takes place, there are likely to be serious deformities unless proper orthopedic and medical treatment has been instituted.

Alex M. Burgess, MD, look at aspects of the treatment of diabetes, stressing the importance of knowledge of the disease and treatment for the general practitioner. Burgess also notes that newer treatments have been successful in increasing the average lifespan of the diabetic patient by nearly forty percent.

Another editorial returns to the evisceration of the chiropractor as a legitimate medical professional. Now the “irregular practitioner” has taken advantage of new technology in the form of x-ray machines in a pseudoscientific manner in order to impress certain types of patients. In particular, they pounce upon any small chance irregularity in an x-ray in which a patient in laying and claim it to be an indication that the spine is “out of plumb” and in need of their brand of treatment.

**Fifty Years Ago, August, 1962**

George J. Garceau, MD, presents a piece on congenital muscular torticollis subtitled “Hematoma, fact or myth?” His study concludes that the theory of simple faulty position in utero, as a cause of congenital muscular torticollis, is not supported by the evidence available, and that hematoma has never been observed to produce torticollis. The theory of ischemia, partial and temporary, of the lower two thirds of the sternocleidomastoid muscle, and the role of the ansa cervicalis nerve deserves further investigation. The author signs off by stating that the theory of trauma, hemorrhage, and hematoma should be removed from textbooks and that the hematoma theory appears to be a myth.

Aaron W. Christensen, MD, discusses “Prevention – a Challenge To the Medical Profession” including a look at the need for private-public partnership in dealing with preventing disability. Most work in rehabilitation involves attempts to reverse existing disabilities, a very high percentage of which could have been prevented in the first place. He asks how physicians could change the picture and how public health officials can help. In regards to the patient, he writes, “If prevention is our goal, we must deal at the outset, not merely as a whole. Does he understand the importance of exercise? Is he motivated to keep them at them regularly, no matter how painful they may be? As the drugs relieve his discomfort, will he slip back to old habits? How can follow up be assured?” The author concludes noting that while he has asked many questions, he is confident that as physicians think about the issues and exchange views, that useful patterns will emerge.

A news item presents a statement from the Council on Foods and Nutrition of the American Medical Association in response to the sale and distribution of confections and carbonated beverages in school lunchrooms. “The availability of confections and carbonated beverages on school premises may tempt children to spend lunch money for them and lead to poor food habits. Their high energy value and continual availability are likely to affect children’s appetites for regular meals.”

**Twenty-Five Years Ago, August, 1987**

A call is made for a reassessment of the certificate of need program in Rhode Island in a piece written by H. Denham Scott, MD, MPH, John T. Tierney, MSW, William J. Waters, PhD, Donald C. Williams, MA, and John X. Donahue, MPA. They note that change in the health care field is both rapid and unpredictable, and thus it is not the time to throw away tools, including the certificate of need and its ability to aid in health care cost control and quality assurance. As a part of the 175th anniversary of the medical society, the journal reprints a public lecture from 1804 by Benjamin Waterhouse, MD with the lengthy title [verbatim]: “Cautions to young persons concerning health in a Public Lecture delivered at the close of the Medical Course in the Chapel of Cambridge containing the General Doctrine of Chronic Diseases; shewing the Evil Tendency of the Use of Tobacco upon Young Persons; more especially the Pernicious Effects of Smoking Cigarrs; with observations on the Use of Ardent and Vinous Spirits in general.” The fascinating reproduction closes with, “To conclude. The moral, to be deduced from our whole Lecture is, the necessity of avoiding all predisposing causes to NERVOUS DISORDERS; and obviating the remote causes of CONSUMPTION. Quit then this pernicious habit, I entreat you. Take all your cigarrs and tobacco, and in some calm evening carry them on to the common, and there sacrifice them to health, cleanliness, and decorum. But, should perversity withstand all the arguments adduced, we have yet one in reserve that is irresistible. The dangerous tendency of these practices no one can doubt; therefore, abandon with custom, LEST YOU PIERCE WITH ANGUISH THE HEARTS OF YOUR AFFECTIONATE PARENTS!”
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**MEDICAL ODYSSEYS**
RIMS published this anthology of essays by Dr. Stanley Aronson, Dr. Joseph Friedman, and editor Mary Korr.

**PORTRAIT RESTORATION**
The 1795 portrait of RIMS’ first president, Amos Throop, was restored to optimal condition for public display.

**BICENTENNIAL GALA**
A festive black tie evening of dinner, dancing, and entertainment was held at Rosecliff Mansion in Newport in April.

**ANNUAL MEDICAL Student Awards**
RIMS’ first annual Amos Throop Prize and Herbert Rakatansky Prize were presented to deserving medical students on May 25, 2012.

**NEUROBIOLOGY SYMPOSIUM**
RIMS will sponsor a lecture series this autumn in cooperation with the Brown Institute for Brain Science and the Norman Prince Neurosciences Institute.

**LOBSTER BAKE**
NORCAL will host this July 20 event for RIMS members on the grounds of the Naval War College Museum in Newport.

**NEW RIMS HISTORY**
A new account of RIMS’ history is under the pen of Executive Director Newell Warde, PhD.
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