

Podcast Transcript

Title: The STD Crisis in America: Where We Are and What Can Be Done

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NCTCFP: Welcome to this podcast sponsored by the National Clinical Training Center for Family Planning. The National Clinical Training Center for Family Planning is one of the training centers funded through the Office of Population Affairs to provide training to enhance the knowledge of family planning staff. During this presentation, *The STD Crisis in America: Where We Are and What Can Be Done*, we will be speaking with Dr. Bradley Stoner. Dr. Stoner is board-certified in Internal Medicine and Infectious Diseases. He is an Associate Professor of Anthropology and Medicine at Washington University School of Medicine in St. Louis, Missouri, where he specializes in clinical epidemiology, diagnosis, and treatment of sexually transmitted diseases. He serves as Medical Director of the CDC-funded St. Louis STD/HIV Prevention Training Center, and is also the immediate past president of the American Sexually Transmitted Diseases Association (ASTDA).

NCTCFP: Welcome, Dr. Stoner. We are glad you could join us for this podcast.

BS: Thank you very much. I'm glad to have this opportunity to speak today about STDs in America. I'm an STD clinician and I take care of patients with STDs and also persons at risk for sexually transmitted diseases, and there really is a STD crisis in our country right now.

NCTCFP: Can you help answer a question many are wondering? Is it STD or STI?

BS: I was giving a talk recently at our university in St. Louis and I said sexually transmitted disease, or STD, and a student raised their hand and said, "Dr. Stoner, don't you know the term has been changed? It's no longer STD- it's STI."

I thanked the student for letting me know this and I investigated this some more. It turns out, the term hasn't quite changed. Sexually transmitted disease, or STD, is still a widely accepted term in North America. It replaced an earlier term, Venereal Disease (VD), which we used to use to describe these infections, but as we learned more about them, we began to call them sexually transmitted diseases because we wanted to emphasize the sexual nature of transmission and the opportunity to interrupt transmission through appropriate medical interventions and prevention activities. In the 1990s, the Europeans started to use the term sexually transmitted infection, or STI, primarily because it was seen as less stigmatizing than disease. To say that you have an infection because many of these diseases actually may be indolent, or not cause any symptoms at any point in time, or may have very subtle symptoms. The term STI, or sexually transmitted infection, might imply that asymptomatic infections are not truly diseases in the classical sense, and therefore, people may be less inhibited from seeking care. I think both terms are appropriate. I think it's probably more appropriate to talk about STIs in the long run, but I think we're stuck with the term STD in the short term. The CDC, the Centers for Disease

Control and Prevention, still uses the term STD to describe the infections that we're most concerned about, and I will continue to use that term throughout the podcast today. My feeling is both terms are appropriate. It hasn't quite changed to STI yet, but we're in the process of switching our terminology.

NCTCFP: What is the impact that STD's are currently having throughout various communities in the country?

BS: STDs represent a substantial health challenge facing our country. The current estimates include about 20 million new sexually transmitted infections per year with a total prevalence of about 110 million people infected with a sexually transmitted infection at any point in time. That's a staggering number of people if you think of a population less than 330 million people; a third of them having an STD at any point in time represents a very substantial morbidity. One major problem is that the number of sexually transmitted infections is increasing and we're concerned that steps need to be taken to really stem the tide of these conditions.

STD's do represent a substantial health threat and particularly among young people age 15-24, who are reproductively active members of the population. More than half of the reported STDs occur in this age group so this is a major concern. As well, men who have sex with men, what we call MSM, also represent an at-risk population and we've seen increasing rates in that group as well. There is a substantial burden of disease throughout the US population and I want to start there.

One of the major concerns about this increase in STDs is the burden it places upon young people 15-24 years of age. 53% of the gonorrhea cases were reported among 15-24 year olds, and 65% of the chlamydia cases occurred in this age group. Reproductively active individuals represent an at-risk population so screening is very important to diagnose these infections and get individuals treated before they transmit the infection to other people.

In November of 2015, the CDC released its annual STD surveillance statistics from the previous year. For the year 2014, we were disheartened to learn that the three major reportable sexually transmitted diseases (chlamydia, gonorrhea, and syphilis) all had increases during the previous year. This is a big concern because these diseases run in different circles, and it's a truism to say that if you have an STD you're at risk for other STDs. That's generally true, but in fact, social network analysis shows us that different individuals are at risk for different diseases at different points in time. For example, the median age of chlamydia infection is about 19-20 years old, and gonorrhea and syphilis tend to run in an older age group so the people with chlamydia can get gonorrhea and syphilis, but by and large, these infections tend to be distinct epidemics. For the first time in 10 years, all three of the major reported STDs (chlamydia, gonorrhea, and syphilis) showed an increase over the previous years' time.

NCTCFP: Okay. Can you elaborate on the increase in those major reported STDs?

BS: Chlamydia often causes subtle symptoms in men and women, such as burning during urination in men with a subtle mucoid discharge from the tip of the penis. In females, the infection may be completely asymptomatic. It typically infects the cervix and does not often cause symptoms that can be perceived. Chlamydia rates were up 2.8% in the United States in 2014, over the previous year period, with more than 1.4 million cases reported. I want to point out that this number of cases is the highest number of cases ever reported to the CDC for any infectious condition. It's often said that chlamydia is

the most commonly reported STD, which is true, but it's also the most commonly reported infectious condition in the United States with 1.4 million cases per year.

Gonorrhea, which also causes urethral discharge in men and cervical infection in women, increased 5.1% in 2014 over the previous year. There were 350,000 cases reported. This is a gross underestimate of the number of cases because this only represents the number of people who presented for diagnosis and treatment. We think there are quite a few more people who remain undiagnosed with this condition.

Syphilis, which causes painless ulcerations in the genital tract, but then spreads throughout the entire body and can cause serious complications including eye disease and brain disease, was up 15.1% in 2014 over the previous 12-month period. This represents a really significant increase because many of these individuals are also co-infected with HIV. I'll talk more about each one of these diseases, in turn, in just a couple of minutes.

NCTCFP: Can you tell us more specifically about each one?

BS: I want to start off first by talking about syphilis. Syphilis is a bacterial infection caused by *Treponema pallidum*. This bacteria is called a spirochete, which means it has a spiral or corkscrew shape which viewed under a microscope. Typically, syphilis causes painless ulcers in the anogenital region, followed by the development of a rash on the palms of the hands and the soles of the feet. I mentioned that rates are up 15% nationally, mostly among men who have sex with men, but also we're seeing increasing rates in women, and higher rates of eye disease, what we call ocular syphilis as well as congenital syphilis which is infants who were infected at birth. These are infants who were delivered from mothers who had syphilis and went undetected during pregnancy so I want to mention that as we go through the podcast.

If you take a look at the broad view of syphilis, penicillin was introduced into clinical practice in the 1940s, and syphilis rates came significantly down since that time. By the year 2000, we had reached historic lows in the number of syphilis cases reported. In fact, the CDC was talking about eliminating syphilis from the United States, but about that same time, rates started to go up in men and stayed relatively low in women, and CDC started to track what is called the male to female rate ratio. This is essentially the number of male cases for every female case. Currently, we're looking at a male to female rate ratio of about 12 to 1, and that means there are about 12 cases of male syphilis for every female case. This primarily means male to male transmission pattern which is occurring because of increasing acquisition of sex partners using social network applications, people finding other people who want to have sexual contact, and often there is very little information known about partners before they engage in sexual contact. Many of these individuals are also HIV+, and unfortunately, what we are seeing is a co-epidemic of syphilis and HIV particularly among men who have sex with men.

One of the disturbing things we've seen about syphilis has been the increase in reported ocular syphilis – that is involvement of the eyes. Most typically, it presents as a posterior uveitis or pan-uveitis but can also include optic neuropathy, retinal vasculitis, interstitial keratitis, and anterior eye chamber disease. These individuals typically report vision loss, flashing lights, blurry vision, and cases are being reported in all parts of the country. A recent CDC report of a cluster of cases in Seattle and San Francisco showed that 92% of these individuals were male and 83% were HIV+. It's not clear if this represents a new strain of syphilis which is causing more invasive eye disease, or whether indeed this is just simply greater recognition of ocular invasion of syphilis that's already been going around. The CDC has issued an ocular

syphilis clinical advisory imploring physicians to be on the lookout for syphilitic eye disease in patients who have syphilis and this can occur at any stage of syphilis. The other concern that we have with syphilis is the occurrence of congenital syphilis, and CDC has reported a 38% increase in congenital syphilis rates over the previous 2-year period. For 2012-2014, congenital syphilis increased after several years of decline of congenital syphilis. And this also tracks the syphilis rate among women. We had seen declines in syphilis among women from 2008-2013, and then the rates started to go up so that by 2014 syphilis in women is starting to creep back up. Many women are entering pregnancy with syphilis and are not being detected by their health care providers. Now, a number of women get no prenatal care at all, and it's unfortunate that women are presenting at delivery with syphilis and then their babies are born with syphilis. Some mothers did receive prenatal care and among those who did, 7% were never tested for syphilis, 17% tested negative early in pregnancy and then acquired syphilis before delivery, and 30% were diagnosed with syphilis during pregnancy but received inadequate treatment. Syphilis is a major concern among women as well. Even though most of the cases are occurring in men who have sex with men, we really can't let our guard down among women, particularly women who are pregnant, and that's a major concern for us.

The clinical presentation of syphilis is tricky because patients present with painless ulcers in the genital tract. These ulcers often don't impel people to seek medical care because they're painless and people may not know they're present or recognize them. They may try over-the-counter treatment to deal with the ulcers because they are painless. Eventually, the ulcers go away but the infection spreads throughout the body typically then causing a rash, what we call secondary syphilis, in the palms of the hands, soles of the feet, although the rash can be distributed widely across the body. Also, it's misdiagnosed or misperceived by patients as an allergic reaction or some other problem. The rash itself goes away but the organism is still alive in the body, and that is the problem with syphilis in that it can undergo a long term latent state, or can become neuro-invasive, that is that it can involve the neurological system and cause neurosyphilis, can invade the eyes causing ocular syphilis as we discussed, and it can also affect the heart. Syphilis has a predilection for causing aortic insufficiency; it tends to erode the ascending aorta near the point in which it joins the heart causing a disruption of the aortic valve often requiring valvular replacement. Syphilis is a bad disease, and certainly something we can't let our guard down, so a 15% increase in syphilis rates really does represent a crisis in this condition.

NCTCFP: How about gonorrhea and chlamydia?

BS: Well, gonorrhea is a bacterial infection caused by *Neisseria gonorrhoeae*. It causes, as I mentioned earlier, urethral discharge in males and cervical infection in females, which may or may not present with a perceived vaginal discharge. Many women with gonorrhea are asymptomatic in the sense that they may have cervical inflammation but there's no pain associated with this. Any cervical discharge that may be occurring may be perceived by the patient as a normal physiologic discharge which may be present at any time. Also occurring with gonorrhea is that it can infect the rectum and the oral pharynx so it's very important to screen patients in rectal and pharyngeal sites if they've had exposures in these sites. Increasingly, we need health care providers to ask their patients about sites for exposure because the rectum and the pharynx are important habitats for the gonorrhea organism. Left untreated, this can cause significant complications particularly in women; it can cause pelvic inflammatory disease leading to long term complications such as infertility, tuboovarian abscess, chronic pelvic pain, and other complications. It can also enter the bloodstream in both men and women causing what's called

disseminated gonococcal infection, or DGI. This is essentially a bacteremia- a serious bacterial infection in which the bacteria enters the bloodstream and causes fever, small joint arthritis, and also costules on distal parts of the body so skin lesion, so called dermatitis with presentation of dissemination of gonococcal infection.

Diagnosis of gonorrhea is typically made through nucleic acid amplification tests. These are non-cultured tests, which are extremely sensitive and specific for detecting the organism. They help us diagnose gonorrhea in genital as well as extra genital sites. One major concern with gonorrhea now, though, is the emergence of drug resistance, and the appearance of drug-resistant forms of gonorrhea is very concerning and we're now approaching a time at which many of the medications that we've used to treat gonorrhea in the past are no longer clinically effective. For example, penicillin was routinely used to treat gonorrhea shortly after World War II and within 10 years it was no longer effective. Secondly, the tetracyclines and doxycyclines in particular were used for many years as first line agents to treat gonorrhea - now no longer routinely effective. Fluoroquinolones antibiotics such as ciprofloxacin were routinely used to treat gonorrhea in the 1990s and are now no longer effective because of emergent drug resistance. The organism figures out a way to develop drug resistance against just about every antibiotic class that is used, and now we're at a point in which the cephalosporin antibiotics are really the last bastion of treatment against gonorrhea. I'll talk about treatment of this organism in a minute, but we routinely co-treat gonorrhea with two drugs now to try to prevent the emergence of drug resistance.

Just a few words about chlamydia. Chlamydia is a bacterial infection that is caused by chlamydia trachomatis. It's a little less clinically aggressive when compared to gonorrhea, but causes pretty much the same clinical presentation such as urethral infection in the male, cervical infection in the female, and also rectal infection is increasingly reported with this organism. Left untreated, it causes long-term complications, particularly in women such as tubal scarring and infertility to the point that chlamydia is now thought to be the number one cause of tubal factor infertility in women in the United States.

There is a major detection bias for chlamydia, which means that many more cases are detected in women than men, but this probably represents more of the fact that women are more likely to go to a health care provider for routine medical care in their reproductively active years for either birth control or pap smears, or for other routine health care. Men don't typically go to the doctor and don't seek healthcare, but they do have this infection and detection, I think, is less among men than that of women so that when we see disparities between women and men we probably are looking at a detection bias in under- detection of chlamydia in men leading to persistence of the organism within the general population. Concern about chlamydia includes the fact that most cases, even in men, are subclinical or asymptomatic and many people are unaware that they have the infection. Thus, screening is very, very important for diagnosing all of these infections.

NCTCFP: You mentioned the importance of screening at the beginning of our interview. Can you talk more about STD screening; its impact, components and potential outcomes?

BS: A few words about detection of these organisms. STD screening is very, very important. Screening is when people are checked for an STD before they have any clinical symptoms. For chlamydia, we've pretty much routinized screening for sexually active women under the age of 25 and for older women who have a risk factor such as a new partner, multiple sex partners, or increasingly we're recognizing that people who have a partner who has more than one partner may be at risk particularly for

chlamydia. Now, people may not know if their partner has other partners, but sometimes they suspect that they might. In our clinic in St. Louis, we're starting to ask people questions like: "Do you think your partner has other partners?"

If people say absolutely not, we're finding that the risk of chlamydia is lower than if they say, "Well, I'm not sure." It might be an important component of a clinical exam to ask people what they suspect about their partner's sexual behavior outside of their own personal relationship with that individual.

I just want to say also that some other STDs which are very important are not classically tracked because they're not reportable conditions to the CDC. For example, herpes, which is a very common sexually transmitted infection, is not a reportable condition so we don't have as good diagnostics or at least good tracking of the epidemiology that we do feel that through analyses of initial visits to physicians' offices that herpes rates are up.

Trichomoniasis, which is a condition of parasitic infection caused by *Trichomonas vaginalis*, is also a very common condition but also not reported, or reportable to public health authorities. So our understanding of the epidemiology of the trichomonal infection is a little less robust. Nevertheless, these conditions, and others such as HPV (Human Papillomavirus), public lice, and other less common sexually transmitted diseases lead us to consider that there continues to be a STD crisis in America, and we really have to keep our guard up to prevent the spread of these infections and to promote good sexual health for the general population.

Now, I'd like to talk for a few minutes about what can be done. As health care providers, we're on the front lines dealing with sexually transmitted infections and one of the most important things that we can do is to screen our patients for STDs. First, a sexual history is very important. I know in medical school we don't typically get taught how to take sexual histories and it's sometimes embarrassing or it makes clinicians and patients uncomfortable to ask specific sex-related questions. I think it's critical for us as health care providers, in order to provide the best care for our patients, to be asking these very sensitive and specific questions. I have found in my practice that patients really do want me to ask specific questions, and I often say, "I'm about to ask you some very personal questions and I have to do this in order to provide the best care for you. I do this for all of my patients so this is essential for providing the very best care so that we don't miss any serious complications."

Asking these sorts of questions, asking about partners, protection, about the use of condoms, about paps and STD history – all of these are important components. And we also ask about specific exposures. We want to know about vaginal-penile sex, but we also want to know about same-sex contact. We want to know about oral-genital contact, and we also want to know about anal-genital contact because these are very important components of the STD evaluation. We do recommend screening at all sites that have been exposed, and screening for gonorrhea and chlamydia is essential. Syphilis is a little bit more tricky to diagnose because it's typically based on diagnosed on serological means which requires a blood test so screening of at-risk populations serologically for syphilis, but also doing a good clinical examination and looking for any sort of syphilitic lesions or rash can be a very important component of the clinical exam. Also, co-infection with HIV is an important issue and all patients with STDs who are at risk should be screened for HIV.

NCTCFP: With the new CDC STD Treatment Guidelines, what does the landscape of treatment look like for STDs?

BS: Well, with regards to treatment: For syphilis, the treatment really has not changed in 60 years. Primary treatment for syphilis is the use of penicillin. We use a long-acting form of penicillin, known as benzathine penicillin G 2.4 million units will treat all cases of early syphilis that is any infection of less than one year's duration, and it includes all primary and secondary cases as well as individuals who have what is termed early latent infection. Patients who have been infected for greater than one year, or for patients who the duration of infection is unknown, we recommend three weekly shots of benzathine penicillin G 2.4 million units intramuscularly and this will cure the infection. There's no known drug resistance to penicillin by the treponema organism, the organism that causes syphilis. Patients who are allergic to penicillin can be treated with oral doxycycline 100 milligrams orally twice a day for two weeks if they have early syphilis, and for four weeks if they have late syphilis. The CDC does not recommend this approach unless the patient truly has a penicillin allergy because compliance is very, very important, and even one missed dose can lead to treatment failure.

Patients with ocular syphilis or with neurosyphilis should be treated with intravenous aqueous crystalline penicillin G, 18-24 million units per day, intravenously. The recommendation is 3-4 million units IV every four hours for 10-14 days. In clinical practice, what we do is place a PIC line, which is a peripherally inserted central catheter and then do continuous infusion of about 18-24 million units daily, as opposed to doing 4 million units every four hours which is a little less convenient. The continuous infusion works very well, patients tolerate it quite well and we do treat for 10-14 days. Some clinicians will then give a single dose of benzathine penicillin G 2.4 million units at the end of the 14-day period of IV penicillin in order to extend the treatment duration by another week to make it comparable to the treatment duration for patients who have been treated with IM penicillin for late-latent infection.

For other STDs, it's a little bit different.. Gonorrhea is an infection now that drug resistance is increasingly common and so in order to stave off drug resistance, we are now routinely co-treating all patients with gonorrhea with an anti-chlamydial agent not because we think they have chlamydia, although many of these patients may, but even patients who do not have chlamydia require an anti-chlamydial agent in addition to the anti-gonorrhea agent in order to stave off the emergence of drug resistance. It's a theoretical argument that when we co-treat patients with two drugs, we will delay the emergence of drug resistance against the last remaining class of antibiotics we have, which is the cephalosporin class. The recommended treatment for gonorrhea for uncomplicated gonorrhea of the cervix, urethra, rectum, or pharynx is ceftriaxone 250 milligrams intramuscularly single dose plus one gram of azithromycin given orally at the same time. An alternative treatment if ceftriaxone is not available is to use oral cefixime, 400 milligrams orally plus one gram of azithromycin orally, but this regimen is not effective for pharyngeal infections and any patients who are treated with this regimen should undergo a test of cure if they are being treated for pharyngeal gonorrhea using this regimen.

Now, some patients have a very severe penicillin allergy or are allergic to cephalosporin and they should be treated with either gemifloxacin 320 milligrams, single dose, orally plus two grams of azithromycin. Or, alternatively, you can use gentamicin 240 milligrams IM (intramuscularly) plus two grams of single dose azithromycin orally. These recommendations are only to be used for people with severe penicillin or cephalosporin allergy.

All patients with gonorrhea should be retested three months after treatment due to high rates of re-infection. For chlamydia, the recommended treatment is azithromycin 1 gram, oral, single dose, or doxycycline 100 milligrams orally twice a day for seven days. Both azithromycin and doxycycline are

effective against chlamydia, but doxycycline requires treatment twice a day for a week so compliance may be an issue. Alternatively, providers can use erythromycin, levofloxacin, or ofloxacin although there's really no clinical reason to use these medications in favor of the recommended treatments because the recommended treatments are much more user-friendly. The alternatives are all multi-dose regimen for over a week and we have limited compliance with some of the treatment approaches.

Patients with recurring infections should be retreated with the original regimen if poor compliance is suspected. Patients who are thought to have persistent urethritis despite treatment with azithromycin should be considered to have possibly either trichomonal infection or *Mycoplasma genitalium*, which is a newly recognized pathogen which can cause urethritis and they can be treated with alternative regimens such as metranidazole and moxifloxacin.

All of these approaches are included in the CDC STD Treatment Guidelines, which appeared in the Morbidity and Mortality Weekly Report in June of 2015, and this document provides the foundation for recommended treatment for all of the STDs. I failed to mention that patients who have chlamydia also should be retested three months after treatment due to high rates of re-infection either from an untreated partner or from a new partner who has an infection.

NCTCFP: Thank you Dr. Stoner, for this valuable information. Can you spare a few minutes for any closing thoughts or to call out any bright spots?

BS: Well, I'll finish up just by talking about expedited partner therapy. Expedited partner therapy, or EPT, is the provision of medication to a patient to give to a sex partner even though that partner has not been seen or evaluated by a medical professional. This has been shown to reduce reinfection of the index case significantly and represents another option for treating partners who are resistant or unable to come in for evaluation or treatment. It's now legal in most states and should be considered as an option for treating partners for patients with gonorrhea or chlamydia. Just to finish up, I will say that indeed we do have a crisis of STDs in the United States. What can be done about it is increased vigilance, increased surveillance, increased screening, and increased adherence to the CDC Treatment Guidelines which form the basis for appropriate evidence-based treatment for STDs in the United States.

Also, health care providers: please look for the mobile app for the CDC Treatment Guidelines now available for iPhone and Android in the app store. It's free of charge and it's a very user-friendly, ready reference guide to help make clinical decisions about STD treatment.

Thank you very much for your time and attention. Good luck in your fight against sexually transmitted diseases.

NCTCFP: Thank you for listening to this podcast with Dr. Bradley Stoner about STIs. For more information and resources for clinicians, please visit the National Training Centers' website at www.fpntc.org or call the National Clinical Training Center for Family Planning at 1-866-91-CTCFP, that's 1-866-912-8237.