CLINICAL MANAGEMENT RECOMMENDATIONS

Dermatologists' Management Approach to Sexually Transmitted Disease

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Why is This Subject Important?

There has been a massive resurgence of sexually transmitted diseases (STD) in recent years. Based upon public health reporting and epidemiologic models, the global incidence of STDs exceeds one million new cases daily, along with a prevalence of 700 million individuals with genital herpes and external genital warts. 1 In the United States, for example, more cases and higher rates of gonorrhea, syphilis and congenital lues have been reported for five vears in a row (2014-2018).² In Europe, the incidence of syphilis, in particular, has dramatically increased in many countries.3 Some of the consequence of STD include acute morbidity, long term neurologic or cardiac disability, psychic distress, neonatal morbidity and even mortality, and infertility.

Is STD Relevant for Dermatology?

Remember that our specialty was once called "Dermatology and Syphilology." In modern times, both our key journals and our academic centers have de-emphasized STDs, including syphilis, to reflect the evolving focus of dermatological practice.4 However, we are currently faced with a set diseases associated with serious consequences that are simply refusing to disappear. and are even increasing worldwide at alarming rates. Many of these disorders have major manifestations on the

skin or may involve the hair and oral mucosa. Who better than a dermatologist to recognize in high-risk constituencies, and others, that patchy non-scarring hair loss may represent syphilitic alopecia and that annular facial lesions may represent secondary syphilis?⁵ Who is (or should be) most capable of distinguishing condyloma lata from condyloma accuminata? Shouldn't the dermatologist know how to differentiate between the various infectious and noninfectious etiologies of genital ulceration? It is also critical to remember that, although dedicated city/county STD clinics important, the majority (70-80%) of STD cases are actually diagnosed and managed by providers in non-STD clinic settings.2 This could certainly include a dermatology office where patients might present with: a new pruritic eruption (scabies, pubic lice), a generalized non-pruritic rash (secondary syphilis), a few tender papulovesicles on the ankle (gonococcemia), genital vesicles (herpes), or genital papules or ulcers (syphilis, chancroid, granuloma inquinale).

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Diagnostic Pitfalls

Although 66-75% of STD occur in the age range of 15-24, one should never discount the possibility of an STD based solely on

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age. About 40% of those 65-80 years old are sexually active.6 STDs have a wide variability in morphological natural appearance, and co-morbidities (such as co-infection or administration immunosuppressive agents) may further alter "classic" clinical features. Clinicians atypical should be aware of morphologies; examples include: scabies, hypertrophic (or vegetative) genital herpes, and the extra-genital chancre of primary syphilis. Furthermore, it is crucial to remember that STD diagnosis or verification often requires a multi-faceted approach. Appropriate culture, serologic testing, direct microscopic examination of exudate or scrapings, darkfield preparation, and skin biopsy with special or immunoperoxidase stains may be required; as available, molecular diagnostics (polymerase chain reaction, nucleic acid amplification testing and genotyping) may also be employed. In addition, aside from testing those with "lesions" or highly suggestive symptoms, screening tests should be entertained for those who are asymptomatic but at notably increased demographic risk. Screening guidelines, by disease state and crossreferenced by demographic classification (men, women, MSM, pregnant women, and HIV positive), are enumerated elsewhere.⁷

Therapeutic Pearls

Standard STD treatment protocols /guidelines are well documented elsewhere.⁸ This information is available in multiple formats, including: both an Apple and an Android cellphone app, a wall chart, a pocket guide, a freely downloadable print version, and online, as needed. Reviewing all treatment recommendations is beyond the scope of this brief summary, but select items are certainly worth noting.

<u>Early infectious syphilis</u> remains amenable to treatment with intramuscular benzathine

penicillin G in a single dose of 2.4 million units. However, in recent years, there have been intermittent shortages of this antibiotic throughout the world. The second line of treatment for primary, secondary and early latent infectious syphilis is oral doxycycline in a dose of 100mg twice daily for 14 days. A regimen of minocycline 100mg twice daily for 28 days also appears to be as effective, if not more so, compared to benzathine penicillin G.9

A not uncommon presentation of urethral gonorrhea is the so-called "bull head clap," which presents as striking edema of the distal penile shaft, extending into the coronal sulcus, with or without dysuria or urethral Uncomplicated discharge. gonococcal infections are treated with dual, single-dose antibiotic administration: intramuscular ceftriaxone 250 mg plus azithromycin 1.0g orally. Treatment of gonorrhea has been complicated by the development antimicrobial resistance, most recently high level cephalosporin resistance, especially in Europe (Spain, France) and Asia (Japan).8 Apparent treatment failures should be immediately referred to specialized STD clinics for further investigation and therapy.

Herpes simplex type 2, the most common cause of herpes progenitalis, typically remains sensitive to acyclovir and its analogues. Ongoing suppressive therapy (e.g. valacyclovir 500-1000mg daily) has multiple benefits. These include: reduction in overt outbreaks, reduction in frequency of asymptomatic viral shedding and reduced disease transmission to sexual partners. 10 Because acyclovir can precipitate in the renal tubules leading to kidney damage. each dose should be taken with a full 8 ounce glass of water. While acyclovir resistance is exceedingly rare in normal hosts, co-infection with HIV may lead to resistance rates ranging from 2.5-16%.11

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Treatment of persistent, acyclovir-resistant infections requires creative intervention, such as application of ophthalmic trifluridine, compounded 1% cidofovir, or 5% topical imiquimod; cryosurgery or electrosurgery; intravenous foscarnet or combinations of the above.¹²

The diagnosis of anogenital warts is usually made by visual inspection, although a confirmatory biopsy is indicated if lesions are atypical (e.g., pigmented or indurated).8 Systematic reviews and metaanalyses of therapeutic modalities are quite difficult due to: heterogeneous treatment methods, a high degree of bias in many studies, and considerable statistical overlap results. 13 among Thus. numerous publications fail to establish a clear hierarchy, therapeutic especially when clearance rates, recurrence rates and risk of events considered are all concurrently. The best recommendation is likely to administer both locally destructive (cryosurgery, treatment electrosurgery. trichloroacetic or bichloroacetic acid, or laser ablation) in combination with topical immunotherapy (imiquimod 5% or 3.75% creams, sinecatechins 15% ointment, 5% 5flurorouracil cream, or podofillotoxin 0.5% solution). For small numbers of warts, destructive therapy is utilized first followed by several months of topical therapy; for larger numbers of warts, topical therapy is administered initially, followed by ablative intervention, followed by several additional months of topical therapy. 14 As to the precise modality used in each phase of management, that must be individualized and selected based on the number, size, morphology. location. and degree keratinization of warts. Of course, prevention is optimal, and the nanovalent HPV vaccine is highly efficacious in this regard. Several recent alterations in vaccine regimen should be highlighted. Vaccine is now indicated

from age 9 until age 45 (instead of age 26), and only two shots are recommended when the vaccine is given under age 15. A massive retrospective study recently verified the high degree of safety associated with the nanovalent HPV vaccine.¹⁵

Pubic lice can be treated with permethrin 1% cream rinse applied to the affected areas and washed off after 10 minutes or with malathion 0.5% lotion applied to the affected areas and washed off after 8-12 hours. Scabies can be treated with permethrin 5% cream applied to all areas of the body from the neck down and washed off after 8-14 hours. For both pediculosis and scabies, oral ivermectin can be used in a dose of 200 mcg/kg, given twice, two weeks apart.8 For crusted scabies, the following regimen may be utilized: 5% topical permethrin cream (full-body application to be repeated daily for 7 days then twice weekly until cure), and concomitant administration of oral ivermectin mcg/kg) on days 1,2,8,9, and 15; (200 additional ivermectin treatment on days 22 and 29 might be required for severe cases. 16

<u>Chancroid</u> and <u>donovanosis</u> are currently vanishingly rare in the United States. Lymphogranuloma venereum has enjoyed a resurgence due to a new serovar (L2b), and may present as perirectal itching, discharge or erosion. This disorder remains sensitive to oral doxycycline (100mg twice daily).

Additional Considerations

Most often, partners are notified by the index case, although public health authorities usually perform epidemiologic tracing and notification for syphilis. Expedited partner therapy (index case is given drug or a prescription for use by sexual contacts) should considered under be the where this circumstances strategy is allowable by law. All persons who seek evaluation and treatment for STDs should

be screened for HIV infection; such screening should be routine, regardless of whether or not the patient reports any specific behavioral risks for HIV infection.8 HIV testing, however, must be voluntary and free of coercion. Clinicians must also report STD cases diagnosed in the private or academic setting to public health authorities. as required by state law. Finally, barrier protection (condom use) should recommended for those who contract an STD, understanding that failure rate due to slippage or breakage is about 1-2%, even with proper use; sex acts for which lubricant was used have a lower failure for both anal and vaginal sex. 17

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