56th Annual Meeting of American Academy of Dermatology

Dermatology and the Information Superhighway

reported by Dr. L.Y. Chong

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Organizer: AAD

In this symposium, the participants learned how to navigate on the internet and integrate the computer into their daily practice. They were also given a perspective on future operations and implications on the information superhighway, including the risks of traveling in Cyberspace and the legal aspects.

Internet has now provided a convenient and important means for communication and interaction between patients, medical personnel, educational institutes and commercial enterprises. Its applications in medicine have grown at an explosive speed and have been more and more widely used. Telemedicine is particularly suitable for those visually-oriented specialties such as dermatology, pathology and radiology. In teledermatology, one could provide real-time, live and interactive consultation for rural and medically isolated areas, where there may not have the specialists available. In the world wide web, even more wide applications have been implemented. These include online patient support groups, public library, medline, electronic publications, conferences and CME, etc. Certain interesting sites had been introduced in the symposium, such as the public library in New Zealand (www.dermnet.org.nz/), free Medline (www.ncbi.nlm.nih.gov/PubMed/), Dermatology Online Journal (http://matrix.ucdavis.edu), Dermatology Online Atlas (www.derma.med.uni-erlangen.de/bilddb/index_e.htm), Global Dermatology Grand Rounds (www.telemedicine.org/rdrugge.htm), etc. The alumni of the St. John's Institute of Dermatology in London might be interested to know that the monthly meeting of St. John's Dermatological Society and the Royal Society of Medicine (Section of Dermatology) are now accessible through the net (http://derm.medlan.cam.ac.uk/).

Having mentioned about all these advantages of information superhighway, the speakers also discussed about the pitfalls of the net. Cost is obviously a great hindrance to the wide availability of these techniques. Security is still a problem in traveling through the internet. Lots of gray areas in legal aspects are still unsolved, as law making is usually far behind the rapidly developing technique in computer, and different places have different laws. In teledermatology, other problems include poor image quality for accurate visual diagnosis, lack of palpation and inability to perform diagnostic or therapeutic procedures. Finally, the harmonious rapport between doctors and patients, established through face to face consultation and touch in reality, could never be replaced by the machine through Cyberspace.

Learning points:

The cost, security problems and the legal implications are still the hindrances in the development of medicine on the internet.

Therapeutic Hotline

reported by Dr. W.H.W. Wong

Treatment of Pruritus

Speaker: Dr. A.B. Fleischer

There are many causes of pruritus. It may be caused by allergic dermatitis, irritant dermatitis, local skin disease, systemic disease, a behavioral pattern or neurological dysfunction. Pruritus results in scratching which causes more skin diseases and perpetuates the vicious cycle.

Conventional therapy includes emollients and antihistamines. Emollient is useful as a repair of skin barrier and prevent irritant dermatitis. Both sedating and non-sedating antihistamines are useful in their own rights. It is interesting to note that 66% of patients can benefit from placebo effect.

In resistant and protracted cases, Doxepin, a tricyclic antidepressant can be tried. It has a very long half life and its steady state is reached in two to four weeks before the drug becomes clinically effective. Another useful drug is Thalidomide, 100-400mg/day is useful in chronic lichen simplex and nodular prurigo. However it is neurotoxic and highly teratogenic.

Other drugs for treatment of pruritus under investigation include Zafirlucast, Naltrexone and Tacrolimus (FK506). Zafirlucast, a leucotriene receptor antagonist, has been proven that it can modify the inflammatory mediators in asthma. Its role in other atopic disease has yet to be investigated. Naltrexone, an opiate receptor antagonist, is useful in cholestatic pruritus, but dependence should be cautioned. Tacrolimus (FK506), an immuno-suppressant like cyclosporine has been tried topically for pruritus, but its efficacy has yet to be evaluated.

Last but not least, it is useful to remember that topical corticosteroid used so often to treat pruritus can cause contact sensitivity, and may be the reason of treatment failure.

Androgenetic Alopecia in Women

Speaker: Dr. Vera Price

The onset of androgenetic alopecia in females usually starts in their late teens, with normal menstruation and absence of hirsutism. There is diffuse thinning with sparing of the frontal hairline but never baldism as in the male. Androgenetic alopecia is caused by progressive miniaturization of hair follicles over several years. There is reduction of the number of hairs and shortened anagen phase. The net result is shorter and finer hair with the effect of diffuse thinning.

When a female patient presents with androgenetic alopecia, extensive hormonal evaluation is usually not required initially. The clinician should check for menstrual irregularity, infertility, hirsutism, severe cystic acne, galactorrhoea and virilization. If these symptoms and signs are present, hormone profile of testosterone, DHEAS, prolactin and TSH should be screened for ovarian and/or pituitary tumour.

Treatment of androgenetic alopecia includes the use of two new drugs. A biological response modifier which prolongs the anagen phase such as 5% Minoxidil has benefit over the previously available 2% preparation. Systemic absorption is only 1.7 % topical dose, and is safe not to cause any side effects. However this preparation contains more propylene glycol and therefore causes more local irritation. Another drug, Finasteride, a 5-*alpha*-reductase inhibitor for androgen blockade, has been FDA approved in men but not yet in women.

Learning points:

In resistant cases of pruritus, Doxepin and Thalidomide can be tried.

It is important to remember that topical corticosteroid used so often to treat pruritus can cause contact sensitivity, and may be the reason of treatment failure.

Immunosuppression and the Skin

reported by Dr. C.S. Leung

Herpes Simplex Infections

Speaker: Dr. M.C. Douglas

The clinical picture of herpes simplex infection (HSV) in immunocompromised patient depends on the degree of immunosuppression. In HIV infection, when the CD4 count is greater than 200, the HSV infection will have relatively normal behaviour. When the count is less than 200, the infection will consist of more long lasting lesions. When the count is less than 50 to 100, atypical and more extensive lesions occur, often presenting as non-healing erosions and ulcerations. Besides these, there is frequent asymptomatic shedding of the HSV at the perianal area in AIDS patients, even in those without history of perianal herpetic lesions. It is also found that involvement of non-keratinizing intraoral areas is more common than previously thought.

Acyclovir resistance is uncommon in patient who is immunocompetent, yet it becomes more common if the degree of immunosuppression is marked, for examples, in AIDS patients with CD4 count less than 100, in bone marrow allograft receipts, and in severe immunocompromised patients with history of HSV infection treated with acyclovir. The therapeutic action of acyclovir, famciclovir as well as valaciclovir is dependent on the viral thymidine kinase activity. It is found that those resistant viral strains have undergone mutation resulting in absent or diminished thymidine kinase function, hence rendering the three drugs ineffective. Under such circumstances, the drug foscarnet can be used intravenously, as majority of the acyclovir strains would be sensitive to it. Its possible side effects include nephrotoxicity, nausea, vomiting and anaemia. In cases of HSV infection that is resistant to both acyclovir and foscarnet, several modes of therapeutic options are available. These include topical HPMPC (3-hydroxy-2-phosphonylmethoxypropyl cytosine), Imiquimod, Trifluridine ophthalmic ointment and Interferon, etc.

HPMPC (an acyclic nucleoside phosphorate-Cidofovir gel) is another useful topical agent. In contrast to nucleoside analog, its action does not need viral enzymes to exert its action. Hence it may decrease resistance and offer protection to uninfected cells. It possesses a broad spectrum of anti-viral activity, including that of HSV1 and 2, CMV, VZV, EBV, HHV-6, Adenovirus and HPV. The cellular uptake of the drug is rapid, and its intracellular metabolites have long half-life of several days. It is interesting to note that lesions that recur later could become acyclovir sensitive again, hence alternating therapy of acyclovir and HPMPC could be adopted for frequent relapsers. Iritis has been reported to be associated with the use of intravenous Cidofovir for treating CMV retinitis. Up to the present moment, HPMPC is still under research, but it could be obtained for "compassionate use".

Imiquimod is a substance that possesses immunomodulating property, but it has no direct antiviral activity on its own. It acts at the site of application, and induces high levels of interferon and low levels of other cytokines locally. This drug has been approved for the treatment of genital warts. It is found that in guinea pig with HSV infections, the drug is useful in treating both active disease and in decreasing relapses. It may potentially been used as a therapeutic supplement to the HSV vaccines.

Trifluridine ophthalmic ointment had been tried in AIDS patients with mucocutaneous HSV infection with success. Other useful therapies include the use of intralesional interferon, and the combination of physical methods (such as curettage and electrodessication) with antivirals (such as interferon).

Learning points:

The potential treatment alternatives for HSV infection resistant to both acyclovir and foscarnet include topical HPMPC, Imiquimod, Trifluridine ophthalmic ointment and Interferon.

Laboratory Tests in Sexually Transmitted Disease

reported by Dr. N.M. Luk

Date: 11 February 1998
Venue: Yaumatei Skin Center
Speaker: Dr. K.M. Kam
Organizer: Social Hygiene Service , DH;
Clinico-pathological Seminar

DEFINITON OF SEXUALLY TRANSMITTED DISEASE (STD)

In 1917, Britain passed her first Venereal Disease Act which included syphilis, gonorrhea and soft chancre as sexually transmitted diseases. In 1989, The World Health Organization published the laboratory manual which included guidelines of treatment in Neisseria gonorrheae, Chlamydia trachomatis, Syphilis, Genital Herpes Simplex, Haemophilus ducreyi, Granuloma inguinale, Candida infections, Trichomonas vaginalis and bacterial vaginosis. This year, 1998, the Center of Diseases Control (CDC), further expanded the scope of sexually transmitted diseases to cover Human Immunodeficiency Virus infection, genital ulcer, urethritis, cervicitis, vaginal discharge, pelvic inflammatory disease, Human Papillomavirus infection, Hepatitis A and B infection, proctitis, proctocolitis, enteritis, scabies and pediculosis pubis.

The following discussion focuses on some of the important aspects of laboratory tests for the three common sexually transmitted diseases, namely Gonorrhea, Chlamydia trachomatis and Syphilis.

GONORRHEA

Besides culture, Gram stain is a convenient method to diagnose gonorrhea in daily practice. The sensitivity and specificity at different sites are as follows:

Site	% Sensitivity	% Specificity
Male Urethra		
Symptomatic	95- 100	95- 100
Asymptomatic	50- 70	95- 100
Endocervix	40- 60	95- 100
Rectum	40- 60	90- 95*

*Lower specificity due to increased prevalence of N. meningitidis in the rectum, especially in homosexually active man.

However, culture of the organism is still of importance for establishing the antibiotic sensitivity of the strains. Sensitivity for the first line antibiotics such as penicillin and quinolone are done as routine in Hong Kong. Whereas second line antibiotics such as spectinomycin, ceftriazone and tetracycline are done when indicated. In addition, beta-lactamase production is also tested.

Typing of the gonococcal isolates is done for epidemiological study and medico-legal reasons. Serotyping, auxotyping, plasmid typing, chromosomal DNA typing and pulsed-field gel electrophoresis methods are used to differentiate the different strains of gonococci.

CHLAMYDIA TRACHOMATIS

Chlamydia trachomatis is classified into 15 serovars. L1, L2, L3 strains are responsible for Lymphogranuloma Venereum. A, B, Ba and C strains are responsible for ocular trachoma. D - K strains can cause inclusion conjunctivitis and genital disease.

Chlamydia trachomatis exists in two forms: the reticulate bodies and elementary bodies.The reticulate bodies are found as inclusion bodies.The elementary bodies, which are released from cells, are present in large number and are infectious. Nowadays most laboratory tests detect elementary bodies rather than reticulate bodies.

Detection of Chlamydia trachomatis comprises of different methods.Cytologic diagnosis has a sensitivity of 10 - 30% for mildly active trachoma; 90% for neonatal conjunctivitis and 50% for adult conjunctivitis. Culture method has a sensitivity of approximately 100% and specificity of 70 - 90%. The lower specificity is due to the presence of inhibitors in the sample, such as the iron in haemoglobin molecule or the lactobacilli in the vaginal flora.

Non-cultural methods are also employed.Enzyme immunoassay detects lipo-polysaccharides. It is genus specific with a sensitivity of 80 - 90% and specificity of 98 - 99%. Direct fluorescent antibody detects MOMP, which is the outer membrane protein. It is species specific. DNA based probe hybridization technique (DNA-RNA) (Gen-Probe) can detect cryptic plasmid and able to amplify the small amount of genetic material present. It has a sensitivity of 85% and specificity of 99.5%. It suffers from sampling error and false negative result due to presence of inhibitors.Serological tests are only available for C. pneumoniae and C. psittaci. It is not available for C. trachomatis because of high background antibodies in STD population. Antimicrobial susceptibility testing is not yet standardized for routine use.

SYPHILIS

The laboratory diagnostic tests for syphilis made its first debut at the turn of this century: with the first non-specific cardiolipin antigen test developed in 1906. Then, the group treponemal tests was invented in 1941 and finally the specific treponemal pallidum tests became available in 1949. The chronological development of these various tests are listed in Table 1.

Table 1: Chronological development of various diagnostic tests for syphilis.

A. CARDIOLIPIN ANTIGEN TESTS

Complement fixation test

- Wassermann reaction

Flocculation tests

- Kahn
- VDRL (Venereal Disease Research Laboratory)
- RPR (Rapid plasma reagin)
- ART (Automated reagin test)
- RST (Reagin Screen test)
- TRUST (Toluidine blue unheated serum test)

Enzyme immunoassays

- VDRL EIA

B. GROUP TREPONEMAL TESTS

- RPCFT (Reiter protein CFT)
- AF EIA (Axial filament EIA)

C. SPECIFIC TREPONEMAL PALLIDUM TESTS

- TPI (Treponema pallidum immobilization test)
- TPIA (Treponema pallidum immune adherence)
- FTA-Abs (Fluorescent treponemal antibody absorption test)
- IgM FTA-Abs
- TPHA (Treponema pallidum hemagglutination assay)
- EIA (Enzyme immunoassay)
- Immunoblotting

The use of the diagnostic tests for screening and confirmation should be specific as indiscriminate use would lead to unreliable results. The indications for specific syphilis tests are stated in Table 2.

Table 2: Indications for specific syphilis tests.

Assay method	Test	Use
Flocculation	VDRL slide, Unheated serum reagin, Reagin screen, RPR 18-mm circle card, Toluidine red unheated serum	Serologic screening & Treatment monitoring
Hemagglutination (Treponema pallidum (Tp)antigen)	MHA for antibodies to Tp	Confirmation of reactive screening test results
Direct Fluorescent Antibody (monoclonal or absorbed polyclonal Ab- Tp conjugate)	DFA- TP	Definitive diagnosis of Tp in lesional material or tissue sample
Indirect Fluorescent Antibody (polyclonal Ab- human conjugate, human γ chain specific conjugate, Tp Antigen)	FTA- ABS FTA- ABS Double Staining	Confirmation of reactive screening tests results

There are certain problems when using these tests for HIV patients. In HIV positive patients, the antitreponemal antibody production may be delayed or absent. The antibody titre may fall even if cure has not been achieved. There may be loss of antitreponemal antibody in older treated patients. On the other hand, very high level of antitreponemal antibody has been reported without reinfection. The high titre may be a reflection of the B-cell dysgammaglobulinaemia seen in HIV infection. Also, serologic response(anti-cardiolipin antibody titre) to treatment may not occur. The incidence of high titre and biologic false positive reactions is increased in this special group of patients.

Learning points:

In patients with concomitant HIV infection and syphilis, the antitreponemal antibody may be very high or absent.