

Application of Internet in Dermatology: Internet Features and Future

reported by Dr. N. M. Luk

Date:	9 September 1998
Venue:	Yaumatei Skin Clinic
Speaker:	Mr. Francis Ho
Organizer:	Social Hygiene Service, DH

Origin of the Internet

Internet is simply a group of computers or servers connected over the world. In the 50's, its use was limited to the military service and the professionals. Not until the invention of World Wide Web (WWW) and a user-friendly interface in the 80's did Internet gain popularity. In Hong Kong, the 'Net' population grew at a rapid pace. It was estimated to be around 70,000 in 1998.

Web sites

Through the Internet, one could approach different web sites or locations that provide information, entertainment and ordering services. More relevant sites related to our profession are listed below:

CME:

<http://www.hkma.com.hk/hkmacme.htm>

American Academy of Dermatology:

<http://www.aad.org>

HKDV Bulletin:

<http://www.medicine.org.hk/hksdv/bulletin.htm>

SHS Handbook of Dermatology and Venereology:

<http://www.hkmj.org.hk/skin>

Hong Kong College of Nursing:

<http://www.medicine.org.hk/conhk/home.htm>

How to look for web sites in the Internet?

It is very convenient to look up relevant web sites even if one does not have an exact location. This could be done through the 'search engine'. 'Alta Vista' and 'Yahoo' are two famous search engines. One can simply type in the search words or items and within seconds, a

search result will be provided that match your requirement. The more specific the search words provided, the more exact will be the search.

Limitation

Internet are limited by the speed of downloading which is, in turn, depends on the modem speed and the bandwidth of the line. Equally important are the facilities of the Internet Service Provider (ISP). Graphic format usually requires more time to download than text format. On the other hand, if more people are using the same ISP simultaneously, the downloading speed will be delayed.

The future

More lively multimedia presentation is the future direction in Internet development. More 'powerful' software such as the Realplayer enables real-time images and sound while downloading the files.

In future, medical scientific meeting may be attended through the internet and computer at home.

Learning points:

Learning through the Internet will be part of our continuing medical education (CME) in future.

Optimizing the Clinical Management of Psoriasis

reported by Dr. K. H. Mak

Date:	12 November 1998
Venue:	Regal Hong Kong Hotel
Speaker:	Prof. Peter van de Kerkhof
Organizer:	HKSDV; Scientific Meeting

A wide spectrum of antipsoriatic treatments is available nowadays. In the lecture, most of them were discussed including topical, systemic and the combined forms. The pros and cons of each type were well illustrated with the demonstration of various studies.

Topical treatment

Potent topical steroids (class III, IV) are often used because of the fast and dramatic response shown within two to three weeks. Therefore, they are useful in crisis intervention. However, the main disadvantage is the fast relapse or even rebound upon withdrawal. The long term dependence especially in case of widespread disease may lead to the appearance of side effects such as skin atrophy, adrenal suppression, cataract formation, perioral dermatitis and emotional disturbance. Therefore, topical steroid alone is not adequate for maintenance treatment.

Calcipotriol (50ug/g in ointment, cream or lotion) is recommended to be the first line treatment. When it is applied two times daily, 80% of patients show satisfactory response that is maximally seen after two to three months. The main adverse effect is skin irritation. It happens in less than 25% of patients. Less than 5% of patients require discontinuation because of the irritation. There is no evidence of hypercalcemia due to systemic absorption if less than 100g/week of ointment are used. The results of a few studies concerning the long-term use of calcipotriol were demonstrated. A significant decrease in PASI (Psoriatic Area and Severity Index) score was seen in two to four months. The efficacy of Talcipotol (4ug/g), another

vitamin D3 analogue being applied once daily, was shown to be slightly inferior to calcipotriol in a study. Nevertheless, it is also an adequate maintenance therapy in psoriasis.

Systemic treatment

Methotrexate (MTX), given in intermittent basis, is effective in psoriasis. However, there is often relapse after its discontinuation. Despite of this, the speaker recommended drug holiday that can minimize drug accumulation. Liver biopsy is still mandatory when the cumulative dose is greater than 1.5g. However, if there is no other risk factor of liver impairment and the period of consumption of the 1.5g is over 2 years, liver biopsy may be optional.

Cyclosporin A (CyA) is also an effective treatment but should not be used in long term because of the possible irreversible renal damage.

There are two newer forms of phototherapy. The narrow band UVB (310nm) is shown to be more effective than the conventional broad band UVB. It is less erythemogenic and requires more energy for action. Therefore, higher doses are required leading to a more expensive cost. Bath-PUVA is another new form of phototherapy. Trioxalsen (0.1-0.3mg/l) or 8-methoxypsoralen (0.4-4.0mg/l) can be used. When compared to oral PUVA, patients experience less nausea and the risk of development of non-melanoma cutaneous neoplasia may be reduced.

Acitretin, when given 35mg/day, is usually effective in treating the plaque psoriasis. However, this drug alone can only maximally reach a 60-70% efficacy, hence a combined treatment is more desirable. In case of generalized pustular psoriasis or the acrodermatitis continua of Hallopeau, acitretin remains the mainstay of treatment with a dosage of 50-60 mg. The main adverse effects of the drug include teratogenicity, mucocutaneous side effects, abnormal liver function and bone change.

Combination treatment

Combination treatments have been developed resulting in an optimized efficacy and a decrease of side effects. However, the following forms of combination are relatively contraindicated: Acitretin - MTX (both hepatotoxic), MTX - PUVA (immunosuppression enhancing carcinogenicity), CyA - MTX (both immunosuppressive), CyA - Acitretin (possible inhibition of CyA hepatic metabolism by retinoids leading to toxicity), and CyA - PUVA (immunosuppression enhancing carcinogenicity).

The recommended combination treatments are as follows: Acitretin - UVB, Acitretin - PUVA (Re-PUVA), Calcipotriol - Topical steroid, Calcipotriol - Acitretin, Calcipotriol - CyA. In Re-PUVA, 10-15mg Acitretin twice a day is given two weeks in advance. After six weeks of phototherapy with a total UVA dosage of 30-60J/cm², 90-95% patients show good response. This form of combination allows a smaller dose of Acitretin and minimizes the possible side effects. Calcipotriol with topical steroid is also a useful combination. The efficacy is comparable to calcipotriol two times daily and there is less skin irritation. The possible

tachyphylaxis of long-term topical steroid is also prevented. A randomized, double-blinded placebo-controlled study was carried out to find out the effect of addition of calcipotriol ointment to acitretin therapy. The results showed that the combination contributed to the efficacy and reduced the cumulative dose of acitretin to reach marked improvement or clearance, thus minimizing the side effects of the drug. Combination of a low dose CyA (2mg/kg/day) and calcipotriol is found to be effective in treating psoriasis as well. Calcipotriol synergistically inhibits human allogenic mixed lymphocyte and mixed epidermal cell reactions, thus potentiate the immunosuppressive effects of CyA. Therefore, the addition of calcipotriol to CyA can enhance patient response to treatment with an improved risk/benefit ratio.

Learning points:

In treating severe psoriasis with combination treatment, combining MTX with PUVA, CyA with MTX, CyA with Acitretin, and CyA with PUVA are relatively contraindicated and should be avoided.

A Certificate Course on Fungal Infections for Medical Practitioners

reported by Dr. S. Y. Cheng

Date:	28 January 1999
Venue:	Furama Hotel, Hong Kong
Speakers:	Professor E. Glyn V. Evans Dr. David T. Roberts Dr. Margaret Ip
Organizer:	Jointly organized by CUHK & HKSDV

Dermatophytes(60%), Trichosporon spp.(7%), Dematiaceous fungi(10%), Candida(19%) and other types of fungi(4%).

Trichophyton(T.) rubrum(40%) and T. mentagrophytes(18%) are the commonest dermatophytes isolated. The other dermatophytes isolated are : Trichophyton spp. (30%), T. verrucosum (4%), T. tonsurans(3%), Microsporum (M.) audouinii (2%), M. canis(0.3%), M. furfur(1%) and Epidermophyton floccosum(2%). The isolation rate of dermatophytes has shown a seasonal variation with highest rate detected in spring (Mar/Apr) and summer (Jul/Aug).

Epidemiology of fungal infections in Hong Kong

Speaker: Dr. Margaret Ip

The positive yield for fungal culture of skin scrapings or nail clippings in Prince of Wales Hospital is around 40%. These positive cultures consist of

Most of the non-dermatophyte filamentous fungi are non-pathogen. The frequency of isolation of each

species is in the following descending order: Cladosporium spp., Cladosporium carrionii, Exophiala jeanselmei, Fonsecaea pedrosoi, Sporothrix schenckii, Scopulariopsis and Fusarium spp.

Candida can be a pathogen or just a colonizing organism. The most common species identified are Candida(C.) albicans and C. parapsilosis followed by Candida spp., C. tropicalis, C. guilliermondii and C. glabrata.

Mycology, laboratory diagnosis, pathogenesis and epidemiology

Speaker: Professor E. Glyn V. Evans

The pattern of superficial fungal infection is different between the developed and developing countries. In developed countries, fungal infection of scalp and body is less common when compared with feet, nails, palms & soles, and groin. In developing countries, fungal infection of scalp, body and groin is relatively common and it may or may not be related to fungal infection of feet and nails.

Scytalidium dimidiatum is said to be the only pathogenic non-dermatophyte which can cause both skin and nail infection. The other non-dermatophyte moulds do not have the necessary enzymes to invade nails. Therefore, they are only secondary invaders and often co-exist with dermatophyte involved damaged nails. They spread in the same way as dermatophytes but they do not respond to any antifungal agent.

Accurate laboratory diagnosis of fungal infection depends on the method of sampling, preparation of sample for examination, direct microscopy, culture failure rate and interpretation of the culture results. The overall fungal culture failure rate is 30% and it differs between different laboratories and clinical centres. The culture failure rate for nail clippings can range from 4% to 66.7% in 16 clinical centres in UK and the difference is due to quality of sampling. Therefore, it is necessary to take nail sample as proximately as possible and discard outermost subungual debris. Most of the non-dermatophyte mould found are incidental only and its presence does not affect the treatment outcome. Therefore, laboratories should not just report the findings only. They should comment the significance

of these non-dermatophyte moulds.

The conventional method for identification of dermatophytes is cheap, simple and reliable. The disadvantages are : difficult to categorize the atypical isolates into species, the problem of positive fungal element but negative fungal culture and the impossibility for strain typing. Strain typing allows us to determine whether a patient is suffering from reinfection or relapse when there is clinical recurrence after treatment. We can also identify specific strain in particular host groups or certain form of diseases e.g. nail infections. Currently, molecular epidemiological studies of dermatophytes infection are undergoing. Up to present moment, 14 different types (DNA type A-N) of T. rubrum species were identified.

Clinical features of fungal infections

Speaker: Dr. David T. Roberts

Clinical appearance of various types of superficial fungal infection are presented. It is particularly mentioned that the prevalence of skin diseases in HIV+ve patients is high (91.4%). Majority are skin infection (170/331) and out of these, 54% are fungal infections and 20% are viral infections. In nail diseases, superficial white onychomycosis is more specific for HIV+ve patients. The occurrence of the skin infections positively correlates with a CD4 count less than 200/ μ l. We will expect that less severe cutaneous infection will occur with the introduction of triple therapy for AIDS patients.

Antifungal drugs, mode of action, spectrum and resistance

Speaker: Professor E. Glyn V. Evans

There are many topical and oral antifungal agents. The drug efficacy depends on the mode of action, minimum inhibitory concentration(MIC)/ minimum fungicidal concentration(MFC), spectrum activity and drug kinetics.

Most of the antifungal agents act by inhibiting the fungal sterol biosynthesis through inhibition of squalene

epoxidase in initial step e.g. Allylamines, or cytochrome-P450 in last step e.g. Azoles.

Allylamines, by causing both accumulation of squalene and depletion of ergosterol, is fungicidal. Its MIC and MFC levels are equal (0.004µg/ml) which is 500 times lower than that of griseofulvin. After administration, it can be detected in stratum corneum after 24-48 hours and in nails after 1-3 weeks. The tissue level at stratum corneum, nails and hairs is significantly higher than the MIC levels. Its spectrum include dermatophytes, non-candida albicans spp. and moulds.

Fluconazole is widely used to treat candida infection in neutropenic patients. The emergence of fluconazole resistance strains becomes a problem, leading to increasing importance of *C. Krusei* and *C. Glabrata* as invasive pathogens. These resistant strain acts by increasing the cytochrome P-450 level or reducing the azole uptake. Most importantly, previous exposure to fluconazole may render it resistance to itraconazole as well. Fortunately, we do not encounter drug resistance problem in treatment of onychomycosis. However, intermittent therapy theoretically can cause drug resistance, especially fluconazole with exposure of only one day per week.

The treatment failure of onychomycosis can be caused by uneven distribution of drugs, "resistant" form of fungi such as mycellium and fungal spores, dormancy of spores and the formation of dermatophytoma. Therefore, we need a prolonged period of treatment to kill all the spores. Furthermore, dermatophytoma does not respond to any antifungal treatment and surgical treatment is required.

Treatment of fungal infections

Speaker: Dr. David T. Roberts

The results of the *Lamisil vs. Itraconazole* in *ON*ychomycosis (*L.I.O.N.*) study (An analysis of the efficacy, safety, and tolerability of terbinafine versus intermittent itraconazole in the treatment of toenail onychomycosis) are presented in the conference.

This was a prospective, randomized, double-blind, double-dummy, parallel-group study. 496 patients were randomized into 4 treatment groups: continuous

terbinafine 250mg/d for 12 or 16 weeks (T12 or T16) or intermittent itraconazole 400mg/d for 1 week, every 4 weeks, repeated 3 or 4 times (I3 or I4).

The efficacy endpoints included mycological cure (negative microscopy and negative culture), clinical cure (100% toe clearing), clinical effectiveness, and complete cure (both mycological and clinical cures) at 72 weeks. It was found that T12 is similar to T16 in all aspects. In mycological cure rate, both T12 (75.7%) and T16 (80.8%) were significantly better than I3 (38.3%) and I4 (49.1%). For clinical cure rate, T16 (60.2%) was significantly better than I3 (31.8%) or I4 (32.1%). For complete cure rate, T16 (55.1%) was also significantly better than I3 (23.4%) and I4 (25.9%). There were no difference in the adverse effects among different treatment groups. Therefore it was concluded that continuous Terbinafine was more effective than intermittent Itraconazole in treatment of toenail onychomycosis in the *L.I.O.N.* study.

Finally, Dr. Roberts comments about the value of different antifungal agents as follows : Griseofulvin - drug of choice in ectothrix tinea capitis in children; Ketoconazole - no indication for its use; Terbinafine - the most potent antidermatophyte agent; Itraconazole - may be equal to terbinafine in skin infection but not in nail infection; and Fluconazole - not widely studied.

Learning points:

Allylamine causes accumulation of squalene & depletion of ergosterol and hence is fungicidal as compared with other antifungal agents.