A 40 year old woman, originally from sub-Saharan Africa, was referred to dermatology by her general practitioner. She had noticed the appearance of several itchy papules around her mouth five months ago (fig 1). She was otherwise well and had no relevant medical history. She was taking no drugs.

Questions
1 What is the diagnosis?
2 What investigations would you do?
3 How would you treat this condition?
4 What other skin diseases are associated with the underlying disease?

Answers
1 What is the diagnosis?

Short answer
This cluster of papules in a peri-oral distribution is molluscum contagiosum.

Long answer
The diagnosis is molluscum contagiosum infection. Molluscum lesions are small benign pearly papules caused by the molluscum contagiosum virus (MCV), a poxvirus that infects the skin and mucous membranes. Infection is spread by direct contact and is usually self limiting—most infections last a maximum of six to nine months. Molluscum lesions are commonly seen in children (on the face and trunk) and in sexually active young adults (often in the genital area). The infection is more common in warm climates.

After penetrating the skin, MCV infects keratinocytes; an inflammatory response is generated, followed by spontaneous regression. In some people an inflammatory dermatitis develops around the molluscum in the weeks after infection, causing erythema and itching.

Molluscum lesions look like a cluster of papules. The differential diagnoses are broad and include milia, warts, basal cell carcinoma, lichen planus, epidermoid cysts, syringoma, and disseminated cryptococcus infection.

Fig 2 Histology of molluscum contagiosum. C=central crater; D=dermis; E=epidermis; K=keratin plug; M=molluscum body. Image courtesy of Ed Uthman

Molluscum lesions have a unique histological appearance (fig 2). After infection, lobules form as the epidermis grows down into the dermis. Molluscum bodies are cells that are distorted by the replicating virus, which are seen in the epidermis and its overlying keratin plug. In the centre of the papule, the stratum corneum breaks down and releases the molluscum bodies and the keratin plug through a central crater.
2 What investigations would you do?

Short answer
It is unusual to find multiple molluscum lesions on the face of a healthy adult so look for causes of immunocompromise. Investigations should include a full blood count and HIV serology.

Long answer
Molluscum contagiosum is usually diagnosed clinically. If available, dermoscopy can aid diagnosis. Dermoscopy findings include the appearance of a central orifice with the presence of prominent vasculature. Vessels may surround the orifice (crown pattern), extend from the centre outwards (radial pattern), appear as small red dots throughout (punctiform pattern), or present as a mixture of the above. Perilesional inflammation or eczema may also be seen. If necessary, the skin can be biopsied and will show changes on direct microscopy as described in fig 2. Molecular analysis (polymerase chain reaction) of a specimen can also confirm the presence of MCV.

It is unusual for healthy adults to have a prolonged MCV infection on the face and HIV serology should be performed urgently. HIV positive patients may have atypical infections with more papules, which take longer to resolve and may become chronic. They are also more likely to have confluent and “giant molluscum” lesions (>10 mm), which can be a challenge to treat. MCV infection in HIV positive patients often heralds disease progression and is associated with advanced disease and low CD4 counts. In one study of 27 HIV positive patients presenting with molluscum contagiosum, the average CD4 count was 86×10^6 cells/L, the proportion of CD4 positive cells was 5.9%, and CD4 to CD8 cell ratio was 0.10. The authors also noted an inverse association between the CD4 count and the number of molluscum lesions. Unfortunately, this was the case with our patient. Her HIV test was positive, her CD4 count was 90×10^6 cells/L (reference range 500-1700) and her CD4 to CD8 cell ratio was 0.15. The appearance of molluscum lesions was the first indicator of late stage HIV disease.

Complicated MCV infections may also present in patients who are immunocompromised for other reasons (for example, after transplantation) and rarely, in patients with atopic skin disease.

3 How would you treat this condition?

Short answer
Treatment is not usually needed in children or young adults because molluscum contagiosum resolves spontaneously in most cases. In atypical infections topical imiquimod or cryotherapy can be used.

Long answer
A Cochrane review published in 2010 concluded that in healthy people molluscum lesions tend to resolve within months and that there is no firm evidence to support treatment. Treatment is warranted in certain cases, such as multiple lesions on the face or giant molluscum lesions associated with HIV infection. Treatment usually takes the form of topical therapy (using 5% imiquimod, 10% potassium hydroxide, or fluorouracil) or cryotherapy so should be used in the first instance. If these measures are of no benefit, topical cidofovir 1–3% can be used. In HIV positive patients, molluscum lesions usually improve with the initiation of highly active antiretroviral therapy (HAART), although exacerbations can be associated with immune reconstitution syndrome. Most patients respond well to topical or physical treatment, but in the rare cases of refractory molluscum in patients with HIV, the use of intravenous cidofovir and paclitaxel has been described.

4 What other skin diseases are associated with the underlying disease?

Short answer
Skin disease may be the first sign of HIV infection. Cutaneous infections and skin malignancies are more common in HIV positive patients.

Long answer
Skin disease is common in HIV, affecting 80–95% of patients at some stage. Dermatological complications can be difficult to diagnose and treat. The earliest involvement of the skin may be a viral exanthem associated with a seroconversion illness. Inflammatory and infectious dermatoses are more common than in the general population, and skin scrapings and swabs should be sent for analysis to aid diagnosis.

Staphylococcus aureus is the most common bacterial infection. Other common presentations include seborrhoeic dermatitis and xerosis. The box lists mucocutaneous diseases that are associated with HIV infection.

Certain dermatological diseases are indicators of a poor prognosis in patients with HIV. Kaposi’s sarcoma is the most common cutaneous cancer in this population. It is more common in men who have sex with men than in the general population and is associated with human herpesvirus 8 (HHV-8) coinfection. Oral hairy leucoplakia is caused by Epstein-Barr virus and although usually asymptomatic is another marker for disease progression.

The most common mucocutaneous side effects of HAART are lipodystrophy, a drug eruption, and painful paronychia.

Patient outcome
Our patient was treated with HAART and topical imiquimod. She died of complications related to advanced HIV disease six months after she presented to the dermatology department.

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Mucocutaneous diseases associated with HIV infection

Infectious diseases

Bacterial
- *Staphylococcus aureus* or meticillin resistant *S aureus* (MRSA)
- Syphilis
- Bacillary angiomatosis

Fungal
- Candida
- Dermatomycoticosis
- Cryptococcosis
- Histoplasmosis

Viral
- Molluscum contagiosum
- Human papillomavirus
- Herpes simplex virus
- Varicella zoster virus
- Cytomegalovirus
- Epstein-Barr virus (oral hairy leucoplaikia)

Arthropods
- Scabies

Cancer
- Kaposi’s sarcoma
- Lymphoma
- Squamous cell carcinoma
- Basal cell carcinoma
- Invasive cervical cancer

Papulosquamous diseases
- Seborrhoeic dermatitis
- Psoriasis
- Reiter’s syndrome
- Xerosis or ichthyosis

Miscellaneous diseases
- Eosinophilic folliculitis
- Drug eruptions
- Hyperpigmentation
- Lipodystrophy
- Photoeruptions
- Pruritus
- Granuloma annulare
- Aphthous ulcers

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